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★ PHILADELPHIA ★ A.M.A. SESSION ★ June 18-22, 1945 ★

Hoffman's Endocrinology

The growing knowledge of the glandular system and its vital relationship to many of the common disorders met in general practice, have lifted endocrinology from the exclusive sphere of the specialist. Endocrinopathies are today a real problem to be met and solved by the practitioner himself, and in this Dr. Hoffman's *new* book offers assistance so practical, so specific and so up-to-date that it has drawn the full endorsement of foremost authorities and leading medical journals.

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Beautifully illustrated, clinically sound, and complete in basic physiology and laboratory aids, this *new* book leads the way to surer diagnosis and more effective therapy.

By JACOB HOFFMAN, A.B., M.D., Associate in Gynecology, Jefferson Medical College; Pathologist in Gynecology, Jefferson Hospital, Philadelphia. *Foreword by* BROOKE M. ANSPACH, M.D., Emeritus Professor Gynecology, Jefferson Medical College. 788 pages, 6½" x 9½", illustrated, some in colors, $10.00.

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AN ARSENICAL WITH A BRILLIANT RECORD OF EFFECTIVENESS AND SAFETY
MAPHARSEN
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THE TREATMENT OF ROCKY MOUNTAIN SPOTTED FEVER

WITH PARTICULAR REFERENCE TO INTRAVENOUS FLUIDS

A NEW APPROACH TO BASIC SUPPORTIVE THERAPY

GEORGE T. HARRELL, M.D.
WILLIAM VENNING, M.D.
AND
WILLIAM A. WOLFF, PH.D.
WINSTON-SALEM, N. C.

Supportive therapy has not been as effectively used in Rocky Mountain spotted fever as it might be. Several misconceptions, including the idea that intravenous fluids are harmful, have been allowed to remain unchallenged in the literature. Specific therapy with hyperimmune antiserum is not widely used as yet and is usually given too late to be of greatest benefit. Before its efficacy can be evaluated, basic supportive therapy must be better standardized. The usual treatment of the disease consists in general supportive measures and the relief of symptoms.

It is true that poorly directed or unwisely chosen parenteral supportive therapy may prove harmful. Because parenteral therapy has been given to poor advantage in some cases, statements such as the following have been made: "In recent years, many physicians of wide experience with spotted fever have advised against transfusions and intravenous fluids. They have observed that patients receiving this type of treatment do not do so well as those who do not receive this therapy. This advice has been followed . . . and intravenous therapy has not been practiced. We wish to emphasize that there is more danger from overtreatment of these patients than from undertreatment."[1] Topping, an investigator of the greatest ability and experience, states that ". . . an occasional patient will require an additional amount (of fluids) parenterally. This had perhaps better be given by hypodermoclysis rather than intravenously, as there is some clinical evidence that any intravenous therapy is contraindicated."[2] Topping quotes unpublished animal experiments of Parker which support the thesis that fluids are harmful: "We have used glucose in guinea pigs with the usual result, namely, earlier death than in the controls."[3] Martin, reasoning from the pathology of the disease, concludes that "blood transfusions probably also are contraindicated because of the endarteritis. . . . However, if the anemia becomes marked, transfusions may be necessary."[4]

Our experiences with supportive therapy are illustrated by the following cases, selected from those studied during the past three seasons. Our initial results were poor because the therapy was unwisely chosen, but when laboratory procedures were used to control the type and amount of treatment excellent results were obtained.

CASE 1.—A white man aged 45, a sawmill worker, removed 2 ticks from his body. Seven days later he developed headache, followed by a rash which appeared first on his feet. He had high fever and was delirious.

The rectal temperature on admission was 41.1 C. (106.2 F.), the pulse rate 118, the respiratory rate 18, the blood pressure 105/65. The man was well nourished, but acutely ill, mentally confused and restless. The skin was wet with perspiration and was covered with reddish brown macules 2 to 3 mm. in diameter, some of which were hemorrhagic. The lungs were clear. The spleen was firm, smooth and nontender and extended 6 cm. below the costal margin.

The accessory clinical data are summarized in table 1 and chart 1. Among the other relevant findings was a clear spinal fluid with 1 polymorphonuclear and 6 mononuclear cells; the initial pressure was 210 mm. of water; the Pandy test was negative. On admission the blood sugar was 136 mg. per hundred cubic centimeters, the icterus index 7.0; by the thirteenth hospital day the icterus index was 5.5. Four weeks after admission the reticulocyte count was 1.8 per cent. Blood and stool cultures were negative; the blood serum agglutinated Proteus OX_{19} in a dilution of 1:160.

The patient was started on quinine 1.2 Gm. daily by mouth on the fourth hospital day but was made definitely worse; a new crop of skin lesions developed and the drug was discontinued on the seventh day. The patient received intravenous metaphen (10 cc. of a 1:1,000 solution) daily for ten days starting on the eighth hospital day. The temperature remained between 40 C. (104 F.) and 41.1 C. (106 F.) for nine days, gradually dropping to normal by the twenty-fourth hospital day. Pain suggesting thrombophlebitis developed, but measurements of the legs were identical. Hallucinations, hiccup, muscular twitchings and urinary and fecal incontinence were noted. The headache was relieved by repeated lumbar punctures.

Glucose, isotonic and hypertonic saline solution, plasma and blood, calcium and vitamins were given intravenously (chart 1). The blood pressure reached levels as low as 90/45 on the ninth hospital day but always rose after intravenous therapy. Generalized edema accompanied by hypoproteinemia began to appear on the tenth hospital day. Pneumonia developed at the right base on the eleventh hospital day and later spread to the left base; this was treated first with sulfadiazine and then with x-rays.

On the thirteenth hospital day protein replacement therapy consisting of blood and plasma transfusions was instituted. The

From the Departments of Medicine, Pediatrics and Pathology, Bowman Gray School of Medicine, Wake Forest College and the Baptist Hospital.

1. Ong, H. A., and Raffetto, J. F.: Rocky Mountain Spotted Fever: An Analysis of 18 Cases in Children, J. Pediat. **17**: 647-653 (Nov.) 1940.
2. Topping, N. H.: Rocky Mountain Spotted Fever, M. Clin. North America **27**: 722-733 (May) 1943.
3. Topping, N. H.: Rocky Mountain Spotted Fever: Further Experience in the Therapeutic Use of Immune Rabbit Serum, Pub. Health Rep. **58**: 757-775 (May 14) 1943.
4. Martin, D. W.: Rocky Mountain Spotted Fever in Children, J. Pediat. **16**: 468-472 (April) 1940.

edema responded promptly and improvement began. The patient was discharged, afebrile, on the thirty-fourth hospital day.

One month after discharge he had regained his lost weight, but dizziness persisted.

The harmful effects of improperly given intravenous therapy are well illustrated by this case. In spite of careful nursing and attention to diet, with moderate

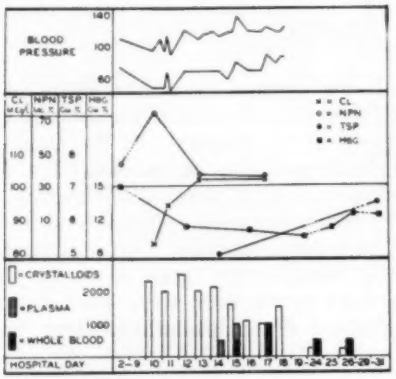

Chart 1.—Effect of intravenous fluids in case 1, man aged 45, rash present four days.

amounts of fluid by mouth, the patient became more toxic. Since he had been sweating profusely, losing water and salt, prerenal azotemia and hypochloridemia developed. These conditions readily responded to intravenous saline and glucose solution, but although the nonprotein nitrogen and chlorides returned to normal the patient clinically was worse. Increasing edema, rales in the lungs and pneumonia developed. The edema was then recognized as being partially due to hypoproteinemia. With the administration of blood and plasma the edema disappeared from the lungs and subcutaneous tissues, and the patient rapidly recovered. Saline solution and glucose were given with impunity after adequate administration of blood and plasma.

The failure of quinine, sulfadiazine and intravenous metaphen as specifics is illustrated. A clinical recrudescence occurred simultaneously with the initiation of quinine therapy.

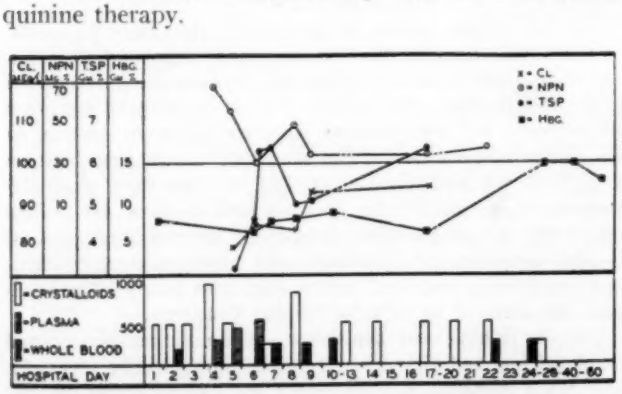

Chart 2.—Effect of parenteral fluids in case 2, girl aged 2 years, weight 11.7 Kg., rash present six days.

The experience with this adult was duplicated in the case of a child:

Case 2.—A tick was removed from behind the ear of a 2 year old white girl two weeks before entry. Headache and high fever developed six days later. A rash appeared on the extremities at the same time and then became generalized.

On admission the child was stuporous and dehydrated with a temperature of 40 C. (104 F.), a pulse rate of 106 and 60 respirations per minute. A generalized petechial macular rash was present, and there were purpuric areas on the toes, heels and elbows. Gallop cardiac rhythm with a soft apical systolic murmur was noted, but there was no peripheral venous engorgement. The lungs were clear. The spleen extended 4 cm. below the costal margin. Occasional muscular twitchings and generalized clonic convulsive movements occurred.

The accessory clinical findings are summarized in table 2 and chart 2. The urine contained many hyaline and granular casts. The spinal fluid was negative. The agglutination for Proteus OX_{19} rose to 1:320. When the serum proteins were 3.4 Gm. per hundred cubic centimeters the albumin fraction was 1.7 Gm. per hundred cubic centimeters, calcium 9 mg. per hunderd cubic centimeters and phosphorus 2.9 mg. per hundred cubic centimeters.

During the patient's first week in the hospital the temperature fluctuated between 37.2 and 40.5 C. (99 and 105 F.), with a disproportionately high, feeble pulse and rapid or Cheyne-Stokes respirations. During the first ten days 1,720 cc. of whole blood, 1,050 cc. of plasma and 2,400 cc. of other fluids (chart 2) were given intravenously or by bone marrow. In five days of treatment the blood chemical findings returned almost to normal. Following the restoration of plasma protein the generalized edema, which had been increasing, disappeared. With the restoration of chloride the convulsive seizures ceased. The patient received, parenterally, ascorbic acid and vitamin B complex during the third week; nutrition was maintained by gavage feeding. By the tenth hospital day the temperature averaged 38.7 C. (102 F.), the pulse 136 and respirations 30

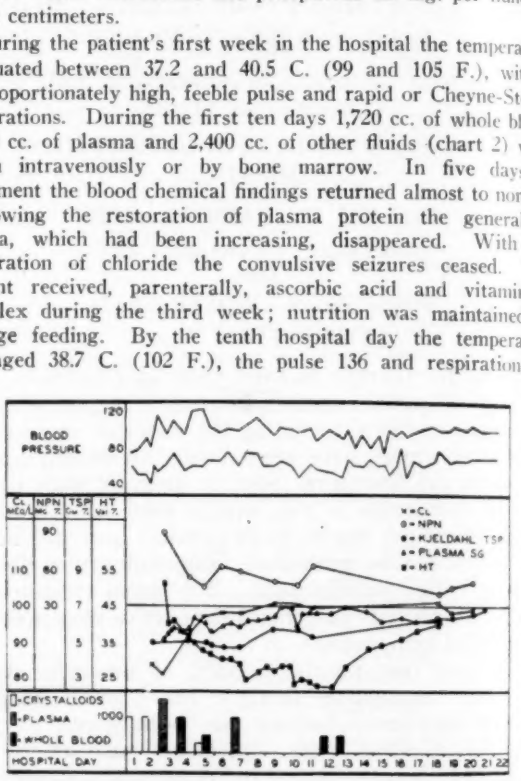

Chart 3.—Effect of intravenous fluids in case 3, boy aged 15 years, rash present eight days. The discrepancy between the values for total serum proteins, as determined by the Kjeldahl method and calculated from values of plasma specific gravity is unexplained.

to 40. The child became afebrile by the fifty-seventh hospital day. Pronounced neurologic changes persisted after clinical recovery; generalized spasticity, mental confusion, choreoathetoid movements of the extremities, hyperactive reflexes and a bilaterally positive Babinski sign were still present at discharge two and a half months after onset.

The anemia and albuminuria present on admission are evidence of the severity of the infection. The severity and persistence of damage to the central nervous system noted in this case occur occasionally in Rocky Mountain spotted fever. Because the patient was comatose, a gavage tube was inserted; the inadequacy of oral fluid and mineral replacement therapy alone is illustrated by the table. Subcutaneously administered parenteral fluids were not absorbed rapidly enough to supplement adequately oral therapy. Prerenal azotemia, edema and hypoproteinemia developed; the loss of protein in the urine contributed to the hypoproteinemia. A dramatic diuresis occurred simultaneously with the initiation of protein replacement therapy given by bone marrow. The tremendous amount of blood and plasma given this 2 year old child

illustrates the safety of properly chosen intravenous therapy. One transfusion of blood from a donor convalescent from the disease was given without reaction.

CASE 3.—A boy aged 15 years complained of a painful postauricular nodule, headache, generalized muscular aching and a sore throat. A rash developed eight days before admission to the hospital. Three days later he had a shaking chill followed by high fever and stupor. No definite history of tick bite was obtained.

day and showed 8 mononuclear cells, a strongly positive Pandy reaction and a negative benzidine test. The agglutination with Proteus OX_{19} became positive in a dilution of 1:640, and the complement fixation test for Rocky Mountain spotted fever was positive in a dilution of 1:32. The van den Bergh test ranged from 2.0 to 1.1 mg. per hundred cubic centimeters. Hippuric acid excretion tests during the first eleven days showed 0.22 Gm. of benzoic acid excreted; by discharge this had increased to 3.00 Gm. Urea clearance tests were at the lower level of the normal range. The nitrogen output in the urine for a period

TABLE 1.—*Clinical Observations in Case 1*

	Blood *								Fluids								Urine		
									Intravenous					Subcutaneous		Oral ‡			
Date †	Hemoglobin, Gm. per 100 Cc.	Red Blood Cells, Millions	White Blood Cells	Hematocrit, Vols. %	Serum Protein, Gm. per 100 Cc.	Nonprotein Nitrogen, Mg. per 100 Cc.	Chloride, mEq. per Liter	Carbon Dioxide, mEq. per Liter	Blood, Cc.	Plasma, Cc.	Water, Cc.	Sodium Chloride, Gm.	Glucose, Gm.	Water, Cc.	Sodium Chloride, Gm.	Water, Cc.	Volume, Cc.§	Specific Gravity	Albumin
9/3/42	15	5.0	7,700	..	...	43	...	..	...	...	.....	..	...	...	..	..	3,700	1,500+	1.018	1+
11	....	...	6,200	..	...	73	82	..	...	...	2,300	27	100	...	..	..	2,450	1,650+	1.016	1+
12	....	...	.....	..	...	..	94	24	...	...	2,000	18	100	...	..	..	2,750	950+	.....	....
13	....	...	.....	..	...	..	...	..	...	...	2,500	23	100	...	..	..	3,100	2,750+	1.010	Trace
14	11	3.2	7,200	..	...	38	102	25	...	...	2,000	18	100	...	..	..	2,250	2,650	.....	....
15	....	...	.....	..	4.9	..	...	..	...	500	2,100	18	100	...	..	..	2,900	1,650+	.....	....
16	....	...	.....	..	...	..	...	..	500	500	1,600	13	75	...	..	..	2,300	3,300+	.....	....
17	....	...	.....	..	...	..	...	..	...	...	1,100	9	50	...	..	..	2,850	3,700+	1.006	0
18	10.8	3.4	4,900	..	...	35	102	..	1,000	...	1,000	9	25	...	..	..	2,400	1,850+	.....	....
19	....	...	.....	..	...	..	...	..	...	...	1,500	13	38	...	..	..	2,400	1,650+	.....	....
25	....	...	.....	..	...	..	...	..	450	...	250	2	...	...	..	..	2,850	1,600+	.....	....
27	11	...	.....	..	...	..	...	..	500	...	200	2	...	...	..	..	2,800	2,600+	.....	....
10/2	12.5	...	.....	..	6.5	..	...	..	...	...	.....	..	...	...	..	..	2,450	2,100+	1.010	0

In the tables * indicates morning values are listed. When other determinations were done during the day, the values are recorded in the graphs.

† Representative days are recorded starting at 7 a. m.

‡ Because of occasional vomiting, the use of enemas and duodenal intubation, the amount of fluid given by the gastrointestinal tract is only approximate in all cases.

§ Each of these patients was incontinent; hence this is only approximate.

TABLE 2.—*Clinical Observations in Case 2*

	Blood *								Fluids								Urine		
									Intravenous					Subcutaneous		Oral ‡			
Date †	Hemoglobin, Gm. per 100 Cc.	Red Blood Cells, Millions	White Blood Cells	Hematocrit, Vols. %	Serum Protein, Gm. per 100 Cc.	Nonprotein Nitrogen, Mg. per 100 Cc.	Chloride, mEq. per Liter	Carbon Dioxide, mEq. per Liter	Blood, Cc.	Plasma, Cc.	Water, Cc.	Sodium Chloride, Gm.	Glucose, Gm.	Water, Cc.	Sodium Chloride, Gm.	Water, Cc.	Volume, Cc.§	Specific Gravity	Albumin
6/19/43	8	3.2	9,040	..	...	..	...	..	...	...	.....	..	...	500	4	25	.....	.....	.....	....
20	....	...	.....	..	...	..	...	..	170	...	.....	..	...	500	..	25	475	.....	.....	3+
21	....	...	.....	..	...	..	...	..	...	...	.....	..	...	500	..	25	1,245	.....	.....	....
22	....	...	.....	..	...	69	...	..	...	300	1,000	..	100	...	..	..	250	.....	.....	....
23	....	...	.....	..	3.4	56	79	26	...	450	500	5	13	...	..	..	175+	.....	.....	2+
24	7	2.6	.....	20	4.6	30	85	..	250	300	.....	..	...	...	..	..	1,040	.....	.....	....
25	8	3.1	13,000	23	6.4	..	...	..	250	...	.....	..	...	250	2	13	375	.....	.....	....
26	8.2	...	.....	31	5.0	48	84	..	...	...	400	..	20	500	5	..	535	.....	1.010	3+
27	....	...	.....	..	5.1	34	93	..	250	...	.....	..	...	...	..	..	415	.....	1.010	2+
28	9	...	12,800	..	...	..	...	..	300	...	.....	..	...	...	..	..	550	.....	1.010	1+
7/1	....	...	.....	..	...	..	...	..	...	...	.....	..	...	500	5	..	1,350	.....	.....	....
2	....	...	.....	..	...	..	...	..	...	...	.....	..	...	500	5	..	625	.....	.....	....
5	7.6	...	21,100	..	6.3	34	94	..	...	...	.....	..	...	500	5	..	620	.....	.....	2+
8	....	...	.....	..	...	..	...	..	...	...	.....	..	...	500	5	..	810	.....	.....	....
10	....	...	.....	..	...	37	...	..	250	...	500	5	25	...	..	..	1,300	.....	.....	....
11	....	...	.....	..	...	..	...	..	...	...	.....	..	...	...	..	..	1,180	.....	.....	....
12	....	...	.....	..	...	..	...	..	250	...	.....	..	...	...	..	..	850	.....	.....	0
16	14.8	...	.....	..	...	..	...	..	...	...	.....	..	...	250	2	13	1,510	.....	.....	....
28	14.6	...	11,300	..	...	..	...	..	...	...	.....	..	...	...	..	..	2,000	.....	.....	0
8/17	12.6	...	14,200	..	...	..	...	..	...	...	.....	..	...	...	..	..	1,060	.....	.....	0

On admission the patient was comatose; his temperature was 38.9 C. (102.5 F.), pulse 104, respirations 28 and blood pressure 80/58. A generalized reddish purple macular rash was present. The eyegrounds showed papilledema. The neck was stiff and painful on motion. The lungs were clear. The spleen was palpable. The liver was not felt. Minimal nonpitting edema of the feet was noted. Sustained ankle clonus was present bilaterally.

The accessory clinical findings are summarized in table 3 and chart 3. On admission, with serum proteins of 4.8 Gm. per hundred cubic centimeters, the albumin was 2.1 Gm. per hundred cubic centimeters. At the time of discharge the albumin-globulin ratio was 1.0. The spinal fluid, which was clear on admission, became xanthochromic by the third hospital of seventy-eight hours was determined. The data indicated the conversion of nearly all the nitrogen to urea. The amount of nitrogen eliminated by the kidney was equivalent to the destruction of 561 Gm. of dry protein, or 7 pounds of skeletal muscle, in seventy-eight hours.

The temperature ranged to 40.4 C. (105 F.), with a corresponding pulse rate, until the twelfth hospital day; it remained around 38 C. (100-101 F.) for ten days longer. With massive intravenous therapy the blood pressure rose to 120/70 but gradually dropped back to 100/60, where it became stabilized. The patient had received 50 cc. of hyperimmune rabbit serum by the fifth hospital day (thirteenth day after the appearance of the rash) without striking change in the degree of toxicity. After the initial dehydration was overcome by intravenous and

subcutaneous infusions, adequate fluids were given by constant duodenal intubation. A high protein, high calory liquid diet, with additional sodium chloride and vitamins, was given by gavage tube. As much as 1,500 cc. of plasma was given intravenously in nine hours. Lumbar punctures relieved the stupor and periodic apnea. The sensorium cleared gradually, but at the time of discharge the neurologic signs had not entirely disappeared.

This case illustrates the life saving property of large doses of plasma in the peripheral circulatory collapse that frequently accompanies severe infections. The great protein requirement is shown by the studies on nitrogen metabolism. No impairment of kidney excretory function was demonstrated. The protein was given ready made, since the liver function studies indicated impairment. The severity of the encephalitis is illustrated by the need for gavage tube feeding, catheterization and lumbar punctures to reduce the cerebrospinal fluid pressure, as well as by the stupor and partial muscular paralysis. Once deficiencies in water and salt were made up by parenteral administration of fluids, an adequate intake was maintained by duodenal intubation even though the patient was comatose.

This was the first case treated in this hospital with specific hyperimmune rabbit serum; little beneficial effect was noted from this, since the disease was well advanced before the patient was admitted.

TABLE 3.—*Clinical Observations in Case 3*

	Blood *								Fluids									Urine		
									Intravenous					Subcutaneous			Oral †			
Date †	Hemoglobin, Gm. per 100 Cc.	Red Blood Cells, Millions	White Blood Cells	Hematocrit, Vols. %	Serum Protein,¶ Gm. per 100 Cc.	Nonprotein Nitrogen, Mg. per 100 Cc.	Chloride, mEq. per Liter	Carbon Dioxide, mEq. per Liter	Blood, Cc.	Plasma, Cc.	Water, Cc.	Sodium Chloride, Gm.	Glucose, Gm.	Water, Cc.	Sodium Chloride, Gm.	Glucose, Gm.	Water, Cc.	Volume, Cc.	Specific Gravity	Albumin
7/11/43	....	5.6	12,500	..	...	..	...	..	...	.....	.....	..	..	1,000	9	..	800	.....	.....	....
12	14	...	.....	..	4.8	..	83	..	...	.....	1,000	9	50	.....	..	..	3,350	1,375+	1.011	0
13	14	5.0	12,200	50	...	88	80	19	...	1,500	.....	..	..	.....	..	..	3,525	1,460+	1.010	0
14	13	4.9	8,200	37	5.0	52	92	19	...	1,000	.....	..	..	.....	..	..	3,050	1,200	.....	....
15	....	...	.....	31	4.8	44	96	19	500	.....	250	2	..	.....	..	..	3,600	2,700	.....	....
16	11.5	4.3	.....	30	4.6	60	97	20	...	.....	.....	..	..	.....	..	..	4,200	4,440	.....	....
17	....	...	.....	29	4.6	57	97	24	...	1,000	.....	..	..	.....	..	..	3,500	3,250	.....	....
18	....	...	.....	26	...	..	...	..	...	.....	.....	..	..	.....	..	..	3,200	2,900	.....	....
19	....	...	.....	26	5.6	47	100	20	...	.....	.....	..	..	.....	..	..	4,400	2,950	.....	....
20	9	3.0	5,600	27	5.6	45	99	19	...	.....	.....	..	..	.....	..	..	4,500	2,500	1.011	0
21	....	...	.....	23	5.2	60	98	16	...	.....	.....	..	..	.....	..	..	4,500	2,400		
22	....	...	.....	22	...	..	...	..	500	.....	.....	..	..	.....	..	..	4,900	2,600		
23	....	...	.....	27	...	..	...	..	500	.....	.....	..	..	.....	..	..	4,800	2,225		
24	....	...	.....	32	...	..	...	..	...	.....	.....	..	..	.....	..	..	4,050	1,400+		
25	10.5	4.4	6,900	33	...	..	...	..	...	.....	.....	..	..	.....	..	..	4,710	2,200		
28	....	...	.....	40	6.1	38	100	22												
29	....	...	.....	..	6.2	42	97	25												
30	12.5	4.3	8,850	..	6.4	46	98	23												
31	....	...	.....	..	6.7	..	96	23												
8/3	....	...	.....	..	6.6	44	99	21												

¶ Kjeldahl method. The values calculated from plasma specific gravity are included in the graph.

COMMENT

Intravenous supportive therapy properly given is not harmful in Rocky Mountain spotted fever but may be life saving. The confusion over this point in the literature has arisen because of failure to appreciate the pathologic physiology of the disease.

Mechanism of the Edema.—Early in the course of the disease a moderate amount of generalized edema involving the face, eyes, hands and legs frequently develops. It is firm in consistency and does not tend to localize in the dependent portions of the body. It is not accompanied by orthopnea. The edema cannot be attributed to cardiac failure, for venous engorgement, rales in the chest and other evidences of cardiac failure are not present. The fatalities are said to result from forced out by the arterial pressure, the protein content of the blood is lowered so that its osmotic pressure on the venous side of the capillary bed is reduced and its ability to hold water in the vascular bed or to draw back fluid from the tissues is lost.

The development of edema is further aggravated by deficient formation of blood protein. Delirium and general intoxication result in a reduced intake of food necessary for the formation of new protein. Because of liver damage, which is a recognized part of the pathology of the disease, protein is not synthesized even though adequate nutrition is maintained. The pronounced reduction of liver function is demonstrated by the hippuric acid studies and by the slightly elevated van den Bergh reaction and icterus index. The extent of this impairment and its significance in relation to therapy has not been sufficiently appreciated. The very large amount of protein metabolized daily is indicated by the nitrogen excretion studies done in case 3. In patients who are stuporous or delirious, tube feeding may be necessary; a high protein, high carbohydrate diet supplemented by casec, if necessary, should be given to protect the liver and to assist in the regeneration of plasma proteins. If liver damage is very severe, ready

"myocardial intoxication" or "renal intoxication," although little evidence has been found post mortem to support this theory. The kidneys are not seriously damaged, as is shown by the urea clearance studies in case 3 and by the ready reduction in blood nonprotein nitrogen when adequate fluids are properly given. Some of the edema, especially that occurring later in the course of the disease, is due to lowering of the plasma proteins.

The disease is not usually diagnosed until after the endothelium and smooth muscle of blood vessels have been damaged, so that the familiar skin eruption results. The injury to blood vessels produces physiologic changes analogous to those caused by burns. Plasma, water and crystalloids leak out of the damaged vessels, producing hemoconcentration and circulatory failure. The tissues of the patient may not be dehydrated, and large volumes of water and crystalloids given by mouth or parenterally may aggravate the situation. With the leakage of fluid,

made protein in the form of blood or plasma should be given intravenously.

Harmful Effects of Intravenous Fluids.—In Rocky Mountain spotted fever one of the most severe forms of peripheral circulatory collapse or "medical shock" develops. The "toxic" condition is strikingly similar to early "shock" associated with functional capillary damage from any cause; experimentally this may be produced by burns, bacterial toxins or other substances. Because of this alteration in the normal physiology of the body it is easy to understand why improperly chosen intravenous fluids would be ineffective and might even be harmful. Since the osmotic pressure of the blood is not maintained, intravenous glucose or saline solution would rapidly leave the blood stream and might even tend to wash more protein out into the tissues. This possibility has been discussed in detail by Minot and Dodd [5] and by Beard and Blalock.[6] The mistaken conception that no intravenous fluids should be used has become entrenched so firmly that even the packages of antiserum contain the admonition "Not to be used intravenously."

The Beneficial Effects of Plasma.—It has been shown by many workers that if "shock" is treated early enough the changes are reversible. Since patients with Rocky Mountain spotted fever present the picture of peripheral circulatory collapse, plasma and whole blood would be the fluids of choice. If the hemoglobin or hematocrit determinations indicate a loss in red cells, whole blood would be preferred until this condition is remedied. We have not observed the severe reactions to transfusions reported by others.[4] Blood or plasma obtained from a convalescent donor seems to have no advantage over that obtained at random. A large quantity of blood or plasma may be required in a short time, as is evidenced by cases 2 and 3. Once the peripheral circulatory collapse and hypoproteinemia are controlled, the proper selection of additional parenterally administered fluids will depend on the hematocrit, blood count and blood chemical studies.

It is conceivable that, in extreme degrees of vascular damage, plasma transfusions may be useless, the plasma passing into the tissues or peritoneal cavity, producing only a transient decrease in the hematocrit and no improvement in peripheral circulation or protein level.[7] It is also conceivable that an overdose of plasma may be given in instances of severe damage. The fluid may not be lost from the body but remain in the tissues and eventually return to the circulation through the lymphatics. The resulting increase in blood volume, as the capillaries recover, might be harmful.

The Proper Use of Crystalloids.—As a result of profuse continued sweating, the blood chlorides may be moderately lowered; muscular tenderness, twitching, fibrillation and convulsions are found, as in heat cramps, and disappear with the restoration of chlorides. Simultaneously prerenal azotemia may occur; this also is common in sublethal shock. In those patients who are treated before the circulatory failure becomes irreversible, no permanent impairment of kidney function results. Crystalloids alone are usually adequate to correct this condition. The solution may be isotonic or hypertonic saline with or without glucose, isotonic solution of three chlorides, calcium chloride, sodium lactate or whatever is necessary. The use of all fluids should be based on the laboratory data and the clinical condition of the patient.[8] In general, the amounts given should be sufficient to restore the circulating blood volume and the blood constituents to normal. Because of the abnormal permeability of the capillaries and the resultant loss of fluids from the vascular tree, repeated laboratory determinations should be made to be sure that the desired result has been obtained. If properly chosen and administered, intravenous therapy is safe and may prove life saving.

Other Methods of Treatment.—Eradication of the infection is made difficult because of the underlying pathology of the disease. The rickettsias are located intranuclearly; hence any therapeutic agent must pass through two cell membranes to reach the organism. It is probably for this reason that the serum recently introduced by Topping [2] has been found to be effective only in the first three days of the rash before a sufficient number of parasites have become established in cells. No specific chemotherapeutic agent is yet available. Quinine and intravenous neoarsphenamine dissolved in a 1:1,000 solution of aqueous metaphen have been used.[9] The sulfonamides have been ineffective and occasionally appear to make the patient worse.[4] Experimentally, guinea pigs treated with sulfonamides died sooner than those which were not treated.[10] Penicillin has not been reported to be helpful.

The liver may be aided in the regeneration of plasma proteins by the intravenous administration of amino acids. The oral vitamin intake can be supplemented by the addition of niacin, ascorbic acid and thiamine hydrochloride to the intravenous injections. The requirement for these substances is increased many times in infections. Thiamine may help prevent shock and hence be especially helpful;[11] ascorbic acid may assist in maintaining the continuity of vascular endothelium.

Treatment of Complications.—Pneumonia is a frequent complication. With the lowering of the blood osmotic pressure pulmonary congestion develops. The protein-containing edema fluid supplies a perfect culture medium for any pathologic organism which may be present in the upper respiratory tract. If the infecting organism does not respond to the sulfonamides or if these are felt to be contraindicated, x-ray therapy may safely be given,[12] as was done in case 1. Penicillin may be useful in such an instance, but we have not yet had an opportunity to try it.

Thrombophlebitis may result from damage to the endothelium of larger blood vessels. The reduction of circulating blood volume, the tendency toward peripheral circulatory failure and the stasis occurring in the presence of vascular damage favor the development of thrombosis. When this occurs in the leg, injection of procaine hydrochloride around the lumbar sympathetic

5. Minot, A. S., and Dodd, Katherine: The Correction of Distorted Fluid Equilibrium in the Presence of Vascular Injury, J. Pediat. **17:** 571-584 (Nov.) 1940.

6. Beard, J. W., and Blalock, Alfred: Experimental Shock, Arch. Surg. **22:** 617-625 (Feb.) 1931.

7. This degree of vascular damage is comparable to that seen in irreversible shock.

8. Wolff, W. A., and Bauer, J. T.: The Control of Fluid Balance by Laboratory Methods, S. Clin. North America **22:** 1759-1774 (Dec.) 1942.

9. Baker, G. E.: Rocky Mountain Spotted Fever, J. A. M. A. **122:** 841-850 (July 24) 1943.

10. Topping, N. H.: Experimental Rocky Mountain Spotted Fever and Endemic Typhus Treated with Prontosil or Sulfapyridine, Pub. Health Rep. **54:** 1143-1147 (June 30) 1939.

11. Govier, W. M.: Studies in Shock Induced by Hemorrhage: III. The Correlation of Plasma Thiamine Content with Resistance to Shock in Dogs, J. Pharmacol. & Exper. Therap. **77:** 40-49 (Jan.) 1943.

12. Rousseau, J. P.; Johnson, W. M., and Harrell, G. T.: The Value of Roentgen Therapy in Pneumonia Which Fails to Respond to the Sulfonamides, Radiology **38:** 281-289 (March) 1942.

ganglions may reduce the pain and prevent the aggravation of restlessness.

For the severe headache, which may be accompanied by actual blurring of the optic disk because of cerebral edema, lumbar puncture to reduce the cerebrospinal fluid pressure may be helpful. Occasionally the changes in the blood supply to the brain may result in temporary mental or neurologic changes which disappear slowly over a period of months, as in case 1, or in more permanent damage to the brain, as in case 2.

Hiccup, probably due to irritation of the central nervous system resulting from vascular injury, may prove extremely resistant to therapy, as in case 1. Heavy sedation with barbiturates, scopalamine or other drugs may be necessary. Occasionally, as a result of damage to the central nervous system, the patient may sleep with his eyes open and develop corneal ulcers. Instillations of some mild substance such as cod liver oil will prevent drying out of the cornea. Herpes simplex may be troublesome but rarely is dangerous. Because of the damage to the blood vessels and the resultant tendency toward anoxia and gangrene, constant and painstaking care must be given to the skin to prevent the development of decubitus ulcers.

SUMMARY

Rickettsial spotted fever is a severe systemic disease. It is rarely diagnosed until the skin rash has appeared. No specific therapeutic agent is available which is effective after the third day of the rash; hence therapy must be largely supportive.

Regulation of supportive therapy, based on the pathologic physiology of the disease, has not been attempted. Because of the vascular lesions, the loss of circulating body fluids, particularly protein, is analogous to that in burns, and peripheral circulatory collapse may develop if inadequate or improper treatment is given. The administration of saline solution or glucose without blood or plasma will aggravate rather than correct the abnormal physiology by washing out further protein.

Intravenous therapy, properly chosen, is not harmful, as it has been reported to be, but may prove life saving. It should include plasma and whole blood in adequate quantities in addition to glucose, salts, vitamins and amino acids. Careful laboratory control in choosing the type and quantity of parenteral or oral fluids to be administered is important.

The elevation of the blood nonprotein nitrogen and lowering of blood chlorides are connectable.

Edema of the subcutaneous tissues and lungs can be produced by excessive administration of crystalloids. The increase in water binding power of the circulating fluid, produced by the administration of blood and plasma, pulls water out of the interstitial spaces and reduces the edema. The peripheral circulation can be supported and the blood pressure raised from shock levels.

The serum proteins are reduced; nitrogen excretion studies suggest that protein destruction is great. The impairment of liver function makes protein replacement therapy necessary for variable lengths of time.[13]

13. After this paper was written a similar study in cases of epidemic typhus was reported: Woodward, T. E., and Bland, E. F.: Clinical Observations in Typhus Fever, with Special Reference to the Cardiovascular System, J. A. M. A. **126:** 287-293 (Sept. 30) 1944.

THE PREOPERATIVE DIAGNOSIS OF PATENT DUCTUS ARTERIOSUS

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MINNEAPOLIS

Since it is now possible to cure a patent ductus arteriosus by surgery it is of utmost importance that the correct diagnosis be made, lest we subject patients unnecessarily to a major surgical procedure or deny those with this lesion the possibility of surgical cure. Since the first successful ligation of a patent ductus by Gross in 1938, patients have been referred to me for surgical treatment, who, on examination, were found to have other types of congenital heart lesions but did not have patent ductus arteriosus. By far the great majority of patients who have come under my observation have not been diagnosed correctly until they were of school age. In most instances these patients were referred to the heart clinic because a murmur was found during the school physical examination. Too often the parents have been told by their family physicians or pediatricians that the child "would outgrow the condition." It is for these reasons that a discussion of the various aspects of the diagnosis of patent ductus arteriosus is both timely and important.

In utero at term, the ductus arteriosus is a vessel of considerable size which acts as a by-pass directing the blood away from the fetal lungs and carrying blood from the pulmonary artery to the aorta. In the normal newborn infant the ductus closes within a few minutes after the first breath is taken. Recent studies [1] suggest that failure of closure in uncomplicated cases of patent ductus arteriosus may result from lack of oxygenation of the blood, possibly because of obstruction of the air passages in the newborn infant.

Two types of patency of the ductus may occur. The duct may remain open as part of a serious developmental defect and may act as the only means of carrying on circulation in a heart seriously impaired by congenital defects. Such patients have unmistakable evidence of congenital heart disease. In the type of case which is curable by surgery the patent ductus is the only defect present. The heart is otherwise normally developed. Strictly speaking the uncomplicated isolated patency of the ductus is not a congenital lesion, as it occurs after birth and has nothing to do with developmental defects of the heart.

SEX AND AGE INCIDENCE

We have had under observation at the clinic for a variable number of years 62 patients in whom a definite diagnosis of uncomplicated patent ductus arteriosus could be made. Of these 62 patients 47 were females and 15 were males (table 2). In all series of cases reported this same preponderance of females is present. This is more than an accidental finding, but there seems to be no clearcut explanation for this sex preponderance.

When our patients were last examined 18 of them were up to 10 years of age, 27 were between 10 and 20 years of age, 10 between 20 and 30, 4 between

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1. Kennedy, J. A., and Clark, S. L.: Observations on Physiological Reactions of Ductus Arteriosus, Am. J. Physiol. **136:** 140-147 (March) 1942.

30 and 40, 1 between 40 and 50 and 2 between 50 and 60 years of age. The 3 patients over the age of 40 have since died. A study of the literature indicates that while patients over the age of 40 with patent ductus arteriosus are occasionally seen, it is true that such patients rarely live beyond this age. As previous studies have revealed,[2] most of them die either of subacute bacterial endarteritis or of congestive heart failure in early adulthood.

Thirty-five of our patients have been observed up to five years, 15 between 5 and 10 years and 12 between 10 and 20 years.

CLINICAL CHARACTERISTICS

Stunting of growth has been considered a typical finding in patients with patent ductus arteriosus. The retardation of growth results from the shunting of blood from the periphery to the pulmonary circulation. However, in my experience stunting of growth is not always found. Some of the more serious cases with definite evidence of cardiac strain have shown no abnormality of growth. Thirty-three of the patients (table 3) have been normally developed, 23 were undersized and 6 were obese.

On physical examination the most characteristic finding in this lesion is the so-called machinery murmur, which is heard over the first or second interspace just to the left of the sternum. The murmur is pathognomonic and, once heard, is easily recognized. The murmur is continuous throughout the heart cycle, and within the murmur an accentuated pulmonic second sound is usually heard. The murmur leads up to the accentuated second sound and then fades away during diastole.

TABLE 1.—*Electrocardiographic Observations*

Normal	52
Left axis deviation (slight)	5
Right axis deviation (slight)	1
Other changes	4

With our present knowledge it is my feeling that a diagnosis of patent ductus arteriosus should not be made unless this characteristic murmur is present. A study of the older literature will reveal the statement that patent ductus arteriosus can occur in patients in whom only a systolic murmur is heard. In my experience all of our patients who have been studied either at the operating table or at postmortem and in whom the diagnosis has been verified have had this characteristic murmur with 1 exception, and in this case no murmur at all was heard. In our series 61 patients had this murmur, while in 1 instance already mentioned in a patient 46 years of age in whom a very large open ductus was found at postmortem no murmur was found.

A thrill, palpable over the point of maximum intensity of the murmur, is usually present. Fifty-three of our patients had this thrill. In 9 instances no thrill was palpable.

The peripheral vascular findings will vary in accordance with the size of the ductus. In patients in whom the ductus is small the pulse pressure may be normal; however, in those individuals in whom there is any considerable leak through the open ductus the peripheral vascular findings will be much the same as those found in aortic regurgitation: increased pulse pressure, pistol-shot femorals, capillary pulse, and the like. In 14 of our patients the pulse pressure was found normal and in 48 there was a definite increase in pulse pressure; in these the accompanying characteristic peripheral vascular findings were noted.

TABLE 2.—*Patients Under Observation*

Cases studied	
Females	47
Males	15
Total	62
Age of patients when last examined	
0 to 10	18
10 to 20	27
20 to 30	10
30 to 40	4
40 to 50	1
50 to 60	2
Number of years followed	
0 to 5	35
5 to 10	15
10 to 20	12

ELECTROCARDIOGRAPHIC FINDINGS

The electrocardiogram in patent ductus arteriosus is important from a negative point of view. In the uncomplicated lesion the electrocardiogram is within normal limits. Occasionally one finds a slight right or slight left axis deviation, and there may also be present slight slurring in one or two leads. However, if a pronounced right axis deviation is found the diagnosis of an uncomplicated patent ductus arteriosus should be seriously questioned. This is also essentially true when a pronounced left axis deviation is found. In our series 52 patients had normal findings (table 1), 5 had a slight left axis deviation, 1 had slight right axis deviation, and 4 had other slight changes.

TABLE 3.—*Clinical Characteristics of 62 Patients with Patent Ductus Arteriosus*

Nutrition	
Normal	33
Stunted	23
Obese	6
Murmur	
Machinery murmur	61
No murmur	1
Thrill	
Present	53
Absent	9
Pulse pressure	
Normal	14
High	48

X-RAY FINDINGS

Roentgen studies are of great value, not only in making the diagnosis, but also in observing the progress of the individual case. Much can be learned in regard to the severity of the leak and the amount of cardiac strain present by x-ray observation. In patients with small ducts the heart may be within normal limits as

2. Shapiro, M. J., and Keys, Ancel: The Prognosis of Untreated Patent Ductus Arteriosus and the Results of Surgical Intervention, Am. J. M. Sc. **206**: 174-183 (Aug.) 1943.

to size. There is almost always a slight enlargement of the pulmonary trunk. The enlargement of the pulmonary trunk may be apparent only on fluoroscopy or by obtaining films in oblique views. In patients with larger ducts and in whom there is considerable leak from the aorta into the pulmonary artery there will be found enlargement of both left and right ventricles as well as moderate to pronounced enlargement of the pulmonary trunk. The branches of the pulmonary artery in the lungs will also be enlarged. On fluoroscopy these pulmonary branches will be seen to pulsate.

In 22 of our patients (table 4) no enlargement of the heart was discovered, 21 had slight enlargement, 15 had moderate enlargement and 4 had pronounced enlargement of the heart. In 10 instances no evidence of enlargement of the pulmonary artery could be made out, 36 had slight enlargement, 15 moderate and 1 pronounced. In 36 instances there was no enlargement of the pulmonary branches, 13 slight, 12 moderate, and 1 pronounced.

TABLE 4.—*X-Ray Observations*

	Enlargement of Heart	Enlargement of Pulmonary Artery	Enlargement of Pulmonary Vessels
None	22	10	36
Slight	21	36	13
Moderate	15	15	12
Pronounced	4	1	1

TABLE 5.—*Diagnostic Verification*

	No. of Cases	Errors
By operation	19	0
By postmortem (3 operative)	7	0

DIAGNOSTIC VERIFICATION

We have had the opportunity of checking our diagnosis in 23 instances (table 5). In 19 patients who have been operated on a patent ductus was found in each instance. Three of these patients died and were further studied post mortem. In the 4 patients who died of this lesion not operated on and were studied post mortem, the diagnosis was correct in each instance, so that up to the present writing no errors in diagnosis have been made in our clinic.

DIFFERENTIAL DIAGNOSIS

There are several cardiac conditions which may be confused with patent ductus arteriosus. One of the most important, especially in infants and young children, is the so-called venous hum. This is also a continuous murmur heard over the base of the heart. It is usually not as loud as the characteristic machinery murmur. The venous hum is generated in the vessels of the neck, may be heard over the base of the heart and not infrequently is heard as far down as the apex. The murmur can be obliterated by moving the child's head from side to side or by applying pressure with the finger on the neck vessels. Of course none of the other findings of patent ductus arteriosus will be present.

Occasionally the diastolic murmur of aortic regurgitation will simulate the machinery murmur. In aortic regurgitation, however, there is invariably a pause between the systolic and diastolic murmurs. These murmurs are usually heard lower down along the left border of the sternum. The blood pressure findings may be exactly the same as in patent ductus arteriosus. X-ray studies, however, will reveal no enlargement of the pulmonary trunk or vessels in the lungs. The enlargement of the heart in aortic regurgitation will, of course, involve primarily the left ventricle, producing a contour which is distinctly different from that found in patent ductus arteriosus. The electrocardiograph in well developed aortic regurgitation will reveal a pronounced left axis deviation.

Patients with interauricular septal defect commonly exhibit x-ray changes which simulate the findings in patent ductus arteriosus. On fluoroscopy the contour of the heart may suggest that found in patent ductus arteriosus; however, in most instances the heart is considerably larger and more rounded in patients with interauricular septal defects. The pulmonary vessels are also usually much larger and pulsate much more in the septal defect. The leak in auricular defect is intracardiac in contrast to that in patent ductus. The peripheral vascular findings in interauricular septal defect are normal, in contrast to the characteristic findings in patent ductus arteriosus. There should be no difficulty in making a differential diagnosis between these two lesions.

In patients with large defects of the interventricular septum, the shunt from left to right may be sufficient to produce enlargement of the pulmonary artery and its branches. The contour of the heart may simulate that in patent ductus arteriosus. In the ventricular septal defect the murmur is not of the machinery type, is heard best at the lower end of the sternum and is not accompanied by the characteristic peripheral vascular findings. The systolic murmur heard over the second left interspace in such instances is produced by the enlarged pulmonary artery and has none of the characteristics of the machinery murmur. Various other types of congenital heart lesions are commonly accompanied by enlargement of the pulmonary artery. Such localized increase in size of the pulmonary trunk in itself is not enough to make a diagnosis of a patent ductus.

DIAGNOSTIC CRITERIA

The diagnostic criteria of patent ductus arteriosus may be summarized as follows:

1. Machinery murmur.
2. Thrill in pulmonary area.
3. Enlarged pulmonary artery.
4. Enlarged and pulsating pulmonary vessels.
5. Enlarged heart.
6. Increased pulse pressure.
7. Stunting of growth.
8. Absence of cyanosis and clubbing of fingers.
9. Normal electrocardiogram.
10. History of heart disease from early childhood.

CONCLUSIONS

1. The diagnosis of patent ductus arteriosus can be made without error.

2. Patients should not be referred for surgical treatment unless they show the characteristic machinery

murmur. The only exception to the rule is the occasional patient with a large patent ductus who may exhibit no murmurs.

3. Patients with cyanosis and clubbing of the fingers do not have uncomplicated patent ductus. They cannot be treated surgically.

4. Pronounced electrocardiographic changes are not part of the picture of simple patent ductus arteriosus.

ABSTRACT OF DISCUSSION

DR. HARRY VESELL, New York: In reference to the murmur in patent ductus arteriosus, in the past several years it has been the general opinion of those who have reported on this subject that the continuous murmur is essential to the diagnosis. I have seen 3 cases in which only the systolic murmur was present. These cases presented the other clinical and x-ray evidence of patent ductus arteriosus. In 1 of them in addition there was subacute bacterial endocarditis, and operation revealed a wide ductus arteriosus but a short one, almost just a fistula. A test I have found of some use in helping to confirm the diagnosis is the one described by Bohn. It is the determination of the blood pressure immediately after exercise. With the blood pressure cuff on the arm, Bohn has a patient do fifteen squats, and within one minute after the end of this exercise he has noted the systolic pressure go up slightly, but the sign he considered pathognomonic is the lowering of the diastolic pressure, which I have seen go down from 60 to 30 or 20. I have found the sign not positive in 1 case in which there was a patent interauricular septum, the diagnosis being proved by angiocardiography. The test has also been confirmed by Lewicki. The first case of subacute bacterial endocarditis on a patent ductus with recovery following operation was reported by Dr. Turoff and myself in 1940. Recent follow-up of these earliest cases reveals that recovery has occurred and four and one-half years after the operation the patients are working.

DR. M. J. SHAPIRO, Minneapolis: I have not seen a proved case of suspected patent ductus arteriosus with only a systolic murmur. I shall still insist on the presence of the typical machinery murmur before a definite diagnosis is made. This is particularly true if surgical treatment is being considered. The results of surgery have not all been good. The mere making of a correct diagnosis of patent ductus arteriosus is not enough indication for surgical intervention. Two of our patients who were operated on developed subacute bacterial endarteritis after surgery. One of them died and the other one has been treated with penicillin and apparently has recovered from his blood stream infection. Until we have accurate statistical data on the effects of surgery, it would be wise to operate on only those patients who show some evidence of cardiac strain or stunting of growth. It is conceivable that in the near future, with the perfection of this surgical procedure, all patients with patent ductus arteriosus might be subjected to surgery, even as a prophylactic measure.

Improvements in Obstetrics During the Eighteenth Century.—With the publication of Mauriceau's text on obstetrics in 1668, this branch of medicine was well on the way to a specialty. Physicians rather than midwives assumed the leading role, and the various medical schools established departments in obstetrics. France, still a leader in the field, produced several able midwives, among whom were Angelique Marguerite Boursier de Coudray and Marie Louise Lachapelle. At the beginning of the century several outstanding obstetricians, who had made a mark in the last decades of the preceding century, were still active—G. Mauquest de la Motte (1655-1737), Hendrik van Deventer (1651-1724), Johann van Hoorn (1661-1721) and Jean Palfyn (1650-1730).—Ricci, James C.: The Genealogy Gynaecology, Philadelphia, Blakiston Company, 1943.

RECENT TRENDS OF LEPROSY IN THE UNITED STATES

REPORT OF SEVEN HUNDRED CASES AT THE NATIONAL LEPROSARIUM

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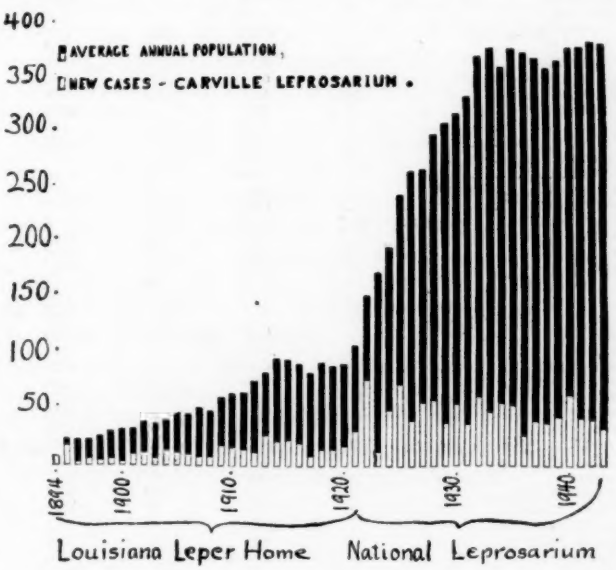
In June 1928 a report was read to the Section on Dermatology and Syphilology of the American Medical Association by Dr. Oswald E. Denney, then officer in charge of the National Leprosarium.[1] In that statistical report special reference was made to the epidemiology of leprosy in the United States, and the



Yearly admissions of new cases and average daily population for fifty years.

trend of the disease in other respects was noted. After a decade and a half this supplemental report is made to show in what respects the present trends are in conformity with those reported fifteen years ago and what new developments have occurred.

INCIDENCE

The number of patients admitted to the National Leprosarium from July 1928 to January 1944 has been 723. This number can by no means be taken as an exact index of the total number of individuals afflicted with leprosy in the United States, nor does the number admitted from any particular geographic area indicate accurately the comparative prevalence of leprosy in that area. However, the large number of cases admitted continuously over long periods of time from some localities do show in a general way a trend toward

Authority given for publication by the Surgeon General of the U. S. Public Health Service, Washington, D. C.
Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.
1. Hopkins, R., and Denney, O. E.: Leprosy in the United States: A Statistical Study of Seven Hundred Cases in the National Leprosarium, J. A. M. A. **92**: 191 (Jan. 19) 1929.

the spread of the disease in those places, while the fact that from other regions few or no cases have been sent to the Leprosarium may be interpreted as showing that in other communities leprosy seldom, if ever, has occurred and that when it did occur it has shown no tendency to spread.

The accompanying chart illustrates graphically the yearly admissions of new cases and the average daily population for each year during the fifty years of existence of a leprosarium at Carville, La.

Table 1 shows the most notable shift in trend has been the increase in the number of cases from Texas, from which more cases have been admitted for the last period than from any other state and from which the annual

TABLE 1.—*States from Which Patients Were Admitted*

	1921 to 1928 Report		July 1928 to January 1944 Report	
	Admissions	Average per Year	Admissions	Average per Year
Alabama	2	0.28	2	0.13
Arkansas	2	0.28	0	0.00
Arizona	1	0.14	6	0.40
California	75	10.71	132	8.80
Colorado	3	0.42	5	0.33
Connecticut	1	0.14	0	0.00
District of Columbia	0	0.00	3	0.20
Florida	34	4.85	49	3.26
Georgia	3	0.42	2	0.13
Idaho	1	0.14	0	0.00
Illinois	11	1.57	17	1.13
Indiana	0	0.00	6	0.40
Iowa	1	0.14	0	0.00
Kansas	1	0.14	1	0.06
Kentucky	1	0.14	2	0.13
Louisiana	423*	12.44	173	11.53
Massachusetts	17	2.42	6	0.40
Maryland	3	0.42	2	0.13
Michigan	8	1.14	7	0.46
Minnesota	6	0.85	2	0.13
Mississippi	8	1.44	5	0.33
Missouri	9	1.28	3	0.20
Montana	3	0.42	0	0.00
Nebraska	1	0.14	1	0.06
New Jersey	5	0.71	3	0.20
New Mexico	0	0.00	1	0.06
New York	41	5.85	79	5.27
North Carolina	1	0.14	0	0.00
North Dakota	1	0.14	0	0.00
Ohio	2	0.28	5	0.33
Oklahoma	1	0.14	3	0.20
Oregon	4	0.57	2	0.13
Pennsylvania	3	0.42	8	0.53
Rhode Island	0	0.00	1	0.06
South Carolina	2	0.28	1	0.06
South Dakota	1	0.14	0	0.00
Tennessee	1	0.14	1	0.06
Texas	31	4.42	183	12.20
Virginia	4	0.57	2	0.13
Washington	3	0.42	8	0.53
Wisconsin	2	0.29	1	0.06
Wyoming	0	0.00	1	0.06

* This figure is the number of cases from Louisiana admitted from 1894 to 1928 and is not comparable with the figures in the same column from other states. During the period 1921 to 1928, 102 patients were admitted from the state of Louisiana, a yearly average of 14.57.

average of admissions is almost three times as great as it was for the first period. Johansen [2] states that there are four main foci of leprosy in Texas: Galveston, San Antonio, Brownsville and Corpus Christi. The number of admissions from Texas now exceeds the number from Louisiana. In former years the largest numbers of cases always came from Louisiana.

From California, New York, Florida and Illinois the average yearly number of admissions, though comparatively large, as may be seen in table 1, has been, like that of Louisiana, remarkably constant for each state for the two periods reported. In New York and Illinois the new cases may have been imported, but from Florida and California there were enough native born admissions to argue for an endemic origin.

2. Johansen, F. A.: Leprosy as a Public Health Problem, Texas State J. Med. **35**: 629 (Jan.) 1940.

In regard to the remaining states, there is not sufficient evidence to show a definite trend in any direction; it can, however, be said that no trend toward the spread of leprosy in these states can be inferred from the small number of admissions to the Leprosarium. In Massachusetts, from which the yearly average declined from 2.42 to 0.40, and in Minnesota, with a decline of 0.85 to 0.13, there is reason to believe that the original foci established by imported cases have now disappeared or are rapidly disappearing.

TABLE 2.—*Nativity of Foreign Born Patients Admitted July 1928 to January 1944*

Mexico	132	British Guiana	1
Philippines	50	Costa Rica	1
British West Indies	22	San Domingo	1
China	17	Panama	1
Russia	9	Malta	1
Hawaii	8	Morocco	1
Puerto Rico	7	Turkey	1
Cuba	6	Syria	1
Greece	6	Portugal	1
Italy	5	Poland	1
Dutch Guiana	4	Norway	1
Virgin Islands	4	Hungary	1
Spain	4	Yugoslavia	1
Brazil	3	India	1
Colombia	3	Korea	1
Canada	3	Tahiti	1
Germany	2		
Japan	2	Total	303

Table 2 shows that from July 1928 to January 1944 the total number of foreign born patients admitted was 303 and that of this number 132 were born in Mexico. The latter number is greater than that of those born in any other foreign country and, considered with the increased number of cases from adjacent Texas, is significant in that it may indicate that much of the leprosy in Texas is directly or remotely of Mexican origin.

From the remaining foreign communities listed in table 2, the majority of patients came from the Philippines, the British West Indies, China, Russia, Hawaii, Puerto Rico and Cuba. In all these countries leprosy is indigenous, and it could well be that patients from them, as well as from the other foreign countries where leprosy is prevalent, could have entered the United States and become naturalized citizens while having leprosy in an unrecognizable stage.

TABLE 3.—*Native Born Patients Admitted from July 1928 to January 1944*

Louisiana	176	Indiana	2
Texas	125	Oregon	2
Florida	34	Arkansas	1
California	23	Maryland	1
Ohio	8	Oklahoma	1
Georgia	7	North Carolina	1
Alabama	5	North Dakota	1
Mississippi	4	Colorado	1
South Carolina	4	Kansas	1
Kentucky	4	Iowa	1
Pennsylvania	4	Massachusetts	1
Arizona	3	Michigan	1
Missouri	3	New Jersey	1
New York	2	Wisconsin	1
Virginia	2		
Total			420

Table 3 shows the states in which patients were born. A comparison of this table with table 1, which shows from which states patients were admitted, indicates that a number of patients born in one state have been admitted to the Leprosarium from another state; for instance, 176 patients were born in Louisiana but only 173 were admitted from that state. Three, therefore,

departed from Louisiana and were admitted from other states.

The difference between the number of patients born in a state and the number of patients admitted from that state is to some extent an indication of the tendency of leprosy to spread. In New York, for instance, with 2 native born admissions and 77 from other states or countries, there is little or no reason to believe that leprosy is endemic.[3] Besides Louisiana, Texas with 125 native born, Florida with 34 native born and California with 23 native born are the other states in which leprosy shows a tendency to spread.

The figures from the state of Texas, which show 58 more patients admitted than were born in that state, are significant when correlated with the great number of patients of American birth but Mexican ancestry admitted from that state. The conclusion seems warranted that a fairly large percentage of these 58 persons contracted the disease in Mexico before their residence in Texas, even though its presence was not discovered until their sojourn in Texas.

Table 4 shows that there have been admitted more patients of Mexican ancestry than patients of other foreign descent. This is additional evidence that leprosy has been introduced from Mexico into Texas and California and, to a less extent, into some other states.

In Table 4 also is to be found evidence, in the large number of patients of Philippine, Chinese and Hawaiian

TABLE 4.—*Racial Ancestry of Patients*

Americans (white 127, Negro 52)	179	Chinese	26
Mexicans	212	West Indian	49
French Canadian	87	South and Central American (Spanish American)	11
Filipino	52	Hawaiian	10
German	41	Asiatic	8
Italian	12		
Other Europeans	36		
Total	723		

ancestry, that leprosy has been introduced directly or indirectly into California from the Philippines, China and Hawaii as well as from Mexico. There is also indication that leprosy has been introduced into Florida, New York and possibly some other Eastern and Southern states from the British West Indies, Cuba, Puerto Rico, Virgin Islands and some Latin American countries.

No admissions are reported of patients born in France, but there are reported 87 of French-Canadian ancestry. The immigrant Acadians, and not the immigrant French, are believed to have been one source of the spread of leprosy in Louisiana. It has been stated that the occurrence of leprosy has been traced back through generations to some of the original Acadian settlers.[4] The continued occurrence of leprosy through many generations of Acadian descendants is considered strong evidence that leprosy is indigenous in Louisiana.

LEPROSY IN THE MILITARY SERVICE

Of significance as to the source from which leprosy is contracted is the different way in which soldiers of the last three wars were exposed to contagion and contracted the disease. There were admitted to the Leprosarium 32 Spanish-American War veterans, 59 veterans of World War I and 10 veterans of World War II. As pointed out by Hasseltine,[5] practically all Spanish-American War Veterans came from nonendemic states and contracted the disease while on military duty on such foreign soil as Cuba, the Philippines and other countries in which leprosy is endemic. On the contrary, those World War I veterans in whom leprosy developed were enlisted into the armed forces from endemic areas in the United States and probably received their infection prior to their entry into military service, which was not to any great extent in countries in which leprosy was prevalent.

TABLE 5.—*Age on Admission*

Ages	No. of Cases
0- 9 years	6
10-19 years	68
20-29 years	170
30-39 years	168
40-49 years	133
50-59 years	95
60-69 years	58
70-79 years	23
80-89 years	2
Total	723

Admissions up to the present time of World War II veterans are, like those of World War I, from states or countries in which leprosy is endemic. Two patients were born in Louisiana, 2 in California, 2 in the Philippines, 2 in Texas, 1 in Mexico and 1 in Puerto Rico. Men in the present military service have not yet been exposed for a sufficiently long time for leprosy contracted in foreign fields to have developed, but the past experience of the Spanish-American War teaches that with the lapse of years, when the long incubation period of leprosy has come to an end, at least a small number of those who have served in countries where leprosy is prevelant will become its victims.

AGE

Table 5 gives the number of patients in each of nine age groups of one decade each. The age is that given at the time of admission and varies in individual cases from 4 to 84 years. The greatest incidence is seen in the twenties and thirties. The average age on admission is 35.5 years.

The average age at onset was computed at 30.4 years, which approximates remarkably closely the average of 30.2 calculated in the 1928 report.

TABLE 6.—*Duration of the Disease Before Admission*

Less than 1 year	121	From 5 to 10 years	146
From 1 to 2 years	128	From 10 to 15 years	55
From 2 to 3 years	95	From 15 to 20 years	30
From 3 to 4 years	81	20 years and over	16
From 4 to 5 years	51		
Total	723		

Table 6 gives the duration of the disease before admission, which was from a few weeks to over forty years according to the histories obtained from the patients. There is calculated to be a lapse of approximately five years in the average case between the onset of the disease and admission to the Leprosarium. This

3. McCoy, G. W.: Observations on the Epidemiology of Leprosy, Pub. Health Rep. **57**: 1935 (Dec. 18) 1942.

4. Aycock, W. L.: Familial Susceptibility as a Factor in Propagation of Leprosy in North America, Internat. J. Leprosy **8**: 137 (April-June) 1940.

5. Hasseltine, H. E.: Leprosy in Men Who Served in United States Military Service, Internat. J. Leprosy **8**: 501 (Oct.-Dec.) 1940.

is significant, as during that time many opportunities for spreading the infection, especially in the home, can be presumed to have existed.

RACE

Of the inmates of the Leprosarium 577 were of the white race, 66 were Negroes, 40 were Filipinos, 10 were Hawaiians and 30 were of the yellow race.

A comparison in native born Louisianians of the incidence in the Negro and the white races shows that there were 34 Negroes and 142 white persons admitted to the Leprosarium during the fifteen year period. The total population of Louisiana in 1940 was 2,363,880. The Negro population amounted to 849,303 and the white to 1,484,467.

The percentage of Negroes in the entire Louisiana population, therefore, was 37.1. The percentage of Negroes admitted to the Leprosarium from Louisiana was 19.3. It seems from these figures that there are approximately half as many Negroes with leprosy in the state in comparison with white persons as might be expected from the ratio of the races to each other in the entire population.

TABLE 7.—*Types of the Disease*

	July 1928 to January 1944		
	Number of Patients	Percentage	1894 to 1928, Percentage
Mixed	329	45.5	49.9
Lepromatous	208	28.6	39.1
Neural	155	21.5	11.0
Tuberculoid	31	4.3	
	723	100.0	100.0

SEX

In the report made in 1928 there were 72.3 per cent males and 27.7 per cent females admitted to the Leprosarium. This percentage is approximately the same as that from almost all countries in which leprosy has been reported, and the incidence in males and females admitted to the National Leprosarium since 1928 is in nearly the same ratio; there were 499 males and 224 females admitted during the last fifteen years, a proportion again of more than two males to one female.

At variance with the almost universal rule of two male leprosy patients to one female patient is the exception found among the native born Negroes, of whom there were admitted 25 men and 27 women. Native born admissions of all races other than Negro showed 246 males and 122 females.

No satisfactory explanation is offered for the almost universal preponderance of males over females nor for the exception found in regard to the Negro race. A correct explanation perhaps would add important knowledge concerning the epidemiology of leprosy. The number of our cases is so small that conclusions should not be drawn from them, but similar findings of an equal incidence in the sexes have been reported by Saunders and Guinto [6] in a field study of leprosy in the Virgin Islands. They cite surveys in Nigeria by Davey and in the Belgian Congo by Degotte, which also showed that prevalence in the sexes was very nearly equal in those countries. It will be noted that the exceptions cited to the rule of incidence in the different sexes have all occurred either in foreign countries with predominating Negro populations or in the United States in the Negro race.

TYPES OF LEPROSY

For the purpose of this report, the classification of cases according to type is given as recorded at the time of admission of the patient.

The recognition of tuberculoid leprosy as a separate type was adopted at the Leprosarium only five or six years ago, and consequently cases reported of this type are less in number and not comparable numerically with those of the other types which are reported for a period of fifteen years.

Table 7 shows the number of cases of each type admitted during the last fifteen years. Percentages of each type for this period are also calculated for comparison with the percentages reported in 1928. In both reports the percentage of cases of the mixed type almost equals the total percentage of lepromatous and neural cases; and in both reports are found a greater percentage of lepromatous than of neural cases.

FAMILY HISTORY OF LEPROSY

Patients admitted to the Leprosarium are usually reticent about disclosing their family relationship because of the fear that, should the information that leprosy existed in their families become generally known, the public knowledge would be detrimental to all their relatives. To avoid this cruel publicity [8] patients in the Leprosarium often live under assumed names, and complete family histories are not always given. Such information as has been obtained, however, is not meager and leads to the conclusion often stated that leprosy is largely a family disease, occurring in closely related persons to an extent that suggests that either there is an inheritable familial predisposition or that the intimate contacts in family life account for the familial incidence. It seems to us probable that both factors play a part in the transmission of leprosy in families.

There were 147 patients with a family history of leprosy. Of these 74 had only one other member of the family afflicted with the disease, 42 had two, 17 had three, 11 had 4, 2 had five and 1 had eight other members of his family with leprosy. The family relationship of the contacts to the patients included 25 fathers, 24 mothers, 2 fathers-in-law, 64 brothers, 36 sisters, 4 sisters-in-law, 1 brother-in-law, 23 uncles, 9 aunts, 19 cousins and 7 grandparents.

In addition to the foregoing there were 24 children, 2 stepsons, 13 nephews and nieces and 7 grandchildren. For statistical purposes these cannot properly be considered as probable sources of family transmission of the disease, though the children and grandchildren might be considered from the point of view of hereditary predisposition.

Besides these there were 16 husbands and wives reported with leprosy, but these do not all indicate marital transmission, as, in all instances except two couples, both persons had the disease prior to marriage.

The comparatively few instances of marital transmission indicate that contact, even prolonged and intimate, is not the only factor in the transmission of leprosy. If the widely entertained view that leprosy is most

6. Saunders, G. M., and Guinto, R. S.: A Field Study of Leprosy in the Virgin Islands, Internat. J. Leprosy **10**: 20 (Dec.) 1942.

8. Leper Loose, Time **42**: 46 (Dec. 6) 1943.

easily contracted in childhood is accepted, and if it is granted that an inherited predisposition plays an important part in familial transmission, the comparatively small number of cases of conjugal infection is readily explained.

OCCUPATION

Employments of patients previous to their admission were listed under one hundred and thirty different occupations, which varied from common laborer to physician. A large majority were in the unskilled labor group, but this majority was not larger than would be expected from the numerical preponderance in normal communities of persons in this group. There were 123 patients classed in the white collar group. As was stated in a previous report, advantages in social status, education, wealth and culture has not insured immunity against leprosy.

INITIAL MANIFESTATIONS

Not all cases, but only those in which a clear history of the onset was obtained are included in the statistics that are now presented.

The first manifestation was recalled as a macule or macules by 259 patients. The situation of the initial macule or macules was on the face in 52 patients, the neck in 4, the body in 29, the arms in 27, the elbows in 2, the wrists or hands in 5, the legs in 47, the buttocks or hips in 9, the knees in 14 and the ankles or feet in 7.

Macules, more numerous and more widely distributed, were remembered as occurring as first lesions on the face and body by 5 patients, on the face and buttocks by 10, on the body and limbs by 16, on the upper and lower limbs by 21, and more or less generalized on various parts of the body by 11.

Nodules were remembered as primary lesions by 193 patients. Of these the face was remembered by 90 patients as being the first site affected, the nose being primarily involved in 14. The ear lobes were reported as the location of first nodules by 4 patients, the body by 7, the buttocks by 1, the legs by 18, the knee by 1, the ankles and feet by 4, the arms by 9, the elbows by 5 and the wrists and hands by 8.

Nodules in multiple sites were recalled as first lesions on the face and body by 4 patients, on the face and limbs by 18, on upper and lower limbs by 15, on body and limbs by 1 and on more or less generalized areas by 8 patients.

Numbness of the hands and feet was the first complaint of 77 patients. Of these 12 first noticed numbness of the fingers, the little and ring fingers being usually the first to be involved. Numbness of the hands and forearms was the first symptom noticed by 23 and numbness of the feet and legs by 42.

Painless burns were noted as the initial symptom by 14 patients: of the fingers or hands by 9, of the feet or legs by 3, of the forearms by 1 and of the elbow by 1.

Swelling of the feet and hands was the mode of onset reported by 23 patients. Swelling of the feet occurred primarily in 7, swelling of the feet and legs in 3, swelling of the hands in 4 and swelling of the hands and feet in 9.

Blisters were the earliest manifestation of leprosy reported by 11 patients, blisters on the fingers or hands being noted by 4, blisters on the feet or toes by 5 and blisters on both hands and feet by 2.

Plantar tropic ulcers were said to be the initial lesion by 5 patients.

There were 4 instances in which the patients reported a paresthesia or peculiar crawling sensation beneath the skin as the first symptom.

Painful neuritis occurring in the limbs was stated to be the earliest indication of leprosy by 4 patients. Loss or thinning of the eyebrows was noted as the first evidence by 4 patients. Two patients reported anhidrosis of the hands and 1 anhidrosis of the feet as the initial manifestation.

There were 26 patients who recalled a chronic nasal catarrh with bleeding, discharge, crust formation and blockage of the nares as their first symptoms. Chills and fever with the outcropping of the lesions similar to those of erythema nodosum was the mode of onset reported by 12 patients.

There is no evidence in the histories of the sites of the initial macules and nodules that would indicate that any one region of the body was the probable port of entry for the infection. The diverse areas enumerated in which the first lesions appeared were the same as those for which the disease showed a predilection as it became more advanced and lesions increased in size and number.

TABLE 8.—*Positive Blood Serologic Reactions in Leprosy*

	Kolmer			Kahn			Combined		
	Number Cases	Number Positive	Per Cent Positive	Number Cases	Number Positive	Per Cent Positive	Number Cases	Number Positive	Per Cent Positive
Mixed.....	312	151	48.4	314	153	48.7	321	181	56.4
Lepromatous.	203	110	54.6	199	110	55.3	206	124	60.2
Neural.....	145	18	11.8	150	21	14.0	152	27	17.7
Tuberculoid...	30	2	6.7	30	3	10.0	31	4	12.9
Total.....	690	281	40.8	693	287	41.4	710	336	47.3

SEROLOGIC TESTS

There is no serologic test of value in the diagnosis of leprosy, but tests intended for the detection of syphilis yield interesting results. That the Wassermann complement fixation reaction and the Kahn precipitation test are frequently positive in leprosy in the absence of syphilis is not sufficiently well recognized by the medical profession.[9] It is not generally known that the serologic reaction is found to vary widely with the different types of the disease.

Table 8 gives the results in the Kolmer and Kahn reactions in different types of leprosy in the group of patients under study. The Kolmer and Kahn tests through long years of experience have been adopted in this institution because they were found to give the least number of false positive reactions in leprosy.

There are 178 patients in whom two to six Kolmer and Kahn tests were made during the course of institutional treatment. All tests were run by the same laboratory technician. It was observed that in the majority of cases the tests remained unchanged throughout the course of the disease, but in 69 patients there was either an increase or a decrease in the degree of the reaction in one or both serologic tests.

It is significant that these changes in serum reactions were closely correlated to changes in the clinical

9. Howard Fox was one of the first in this country to point out that a positive Wassermann reaction is frequently obtained in cases of leprosy in which there is no history or symptom of syphilis. Fox, H.: The Wassermann and Noguchi Complement Fixation Test in Leprosy, Am. J. M. Sc. **139:** 725 (May) 1910.

manifestations of the disease. We believe that this argues for the presence in the serum of leprosy patients of a reagin which reacts positively with Kolmer or Kahn antigen in the absence of syphilis. These figures confirm the previous findings of Badger [10] in this respect and are reported elsewhere in detail.[11]

TREATMENT

All patients with few exceptions received some type of treatment directed against leprosy. More or less routine treatments consisted of chaulmoogra oil given by mouth and intramuscularly, the iodized esters of hydnocarpus intramuscularly, solution of potassium arsenite by mouth, cod liver oil in varying doses, vitamins in various combinations and strychnine sulfate.

Experimental treatments included gold sodium thiosulfate, mercurochrome intravenously, smallpox vaccine, hirudin, fever therapy in the Kettering hypertherm cabinet, diphtheria toxoid, sulfanilamide, sulfathiazole, sulfapyridine, sulfadiazine, promin, Internal Antiseptic 307, diasone, pooled human plasma, Karwinskia latifolia and penicillin. None of the experimental treatments proved specific, but best results with least harmful effects were produced by promin [12] and diasone.

Until a more specific drug can be developed, general hygienic measures including institutional and nursing care, physical therapy, judiciously adjusted hours of rest and outdoor exercise, and especially a well balanced nutritious diet must continue to play an important role in overcoming the disease.

DURATION OF LEPROSY

For all the types of leprosy combined, the average duration of the disease from the time of its onset until death was estimated at 10.3 years for those patients under study who died in the hospital during the period covered by this report. This estimate is approximately four years less than that calculated for the 1928 report, but the shorter period of observation, fifteen years in comparison to 34 years, explains this difference.

Duration of life after contracting the disease varied in the different types of leprosy as follows: neural cases 14.5 years, mixed cases 10.6 years and lepromatous cases 9.3 years. In tuberculoid cases there was only one death, eighteen years after onset.

TABLE 9.—*Disposition of Patients*

	Paroled Patients				Absconded Patients				
Types of Disease	Number of Cases	Discharged, Disease Arrested	Remaining in Hospital, Disease Arrested	Readmitted, Disease Relapsed	Total	Readmitted to Hospital	Aliens Deported to Native Country	Deaths	Patients Remaining in Hospital (1928-1943 Admissions)
Mixed	329	19	3	5	51	24	13	117	161
Lepromatous	208	16	2	2	42	19	13	52	108
Neural	155	90	9	8	13	3	6	20	46
Tuberculoid	31	20	2	0	5	2	0	1	9
Total	723	145	16	16	111	48	32	190	324

The average duration of life in the different types shows, as do other figures in regard to type, that the best prognosis is in the tuberculoid type and that the prognosis is better in the neural cases than it is in either the lepromatous or the mixed cases.

TABLE 10.—*Causes of Death*

	Mixed	Lepromatous	Neural	Total
Nephritis	35	18	2	55
Tuberculosis	21	10	6	37
Leprosy	8	1	0	9
Leprous laryngitis (asphyxia)	13	4	0	17
Heart diseases	9	6	0	15
Pneumonia	9	3	1	13
Septicemia (including gangrene)	4	1	3	8
Malignancy	1	4	3	8
Peritonitis (postoperative)	4	0	1	5
Diabetes mellitus	1	2	0	3
Suicide	2	1	0	3
Meningitis (pneumococcic)	1	1	0	2
Syphilis (cerebrospinal 1) (cardiovascular 1)	1	0	1	2
Cirrhosis of liver	1	0	1	2
Hemorrhage, cerebral	1	0	0	1
Hemorrhage (gastric ulcer)	1	0	0	1
Malaria (pernicious)	1	0	0	1
Cavernous sinusitis	1	0	0	1
Lymphatic leukemia	1	0	0	1
Abscess of lung	1	0	0	1
Asthma (bronchial)	1	0	0	1
Pericarditis, purulent	0	1	0	1
Scarlet fever	0	0	1	1
Arteriosclerosis (gangrene of foot)	0	0	1	1
	117	52	20	189
Calculous obstruction of ampulla of Vater (tuberculoid case)				1
Total				190

DISPOSITION OF PATIENTS

Table 9 shows that 145 of the 723 patients hospitalized, or 20 per cent, have been paroled as having the disease in an arrested form and being no longer a menace to public health.

Criteria in this institution for parole are twelve consecutive monthly negative bacterioscopic examinations of cutaneous and nasal smears and an inspection by the medical staff to determine whether or not there are any visible or palpable signs that the disease is still active.

The better or worse prognosis in the different types of the disease show clearly in the percentages of each type paroled, in the percentages of relapsed paroled patients and in the percentages of deaths occurring in each type.

Table 10 shows the primary causes of the 190 deaths occurring in the Leprosarium among the 723 patients included in this study. The mortality rate was 26.7 per cent, but leprosy was responsible for only a small percentage of the deaths. While nephritis and tuberculosis were the direct cause of almost half the fatalities, it is probable that leprosy was responsible for the occurrence of these two diseases and that the lepromatous and mixed types were more prone to develop these fatal complications than was the neural type. Necropsies confirming the primary cause of death were performed in 75.3 per cent of deaths.

At present there are remaining in the Leprosarium 324 patients who were originally admitted subsequent to July 1, 1928, the date on which the period of the

10. Badger, L. F.: Significance of Positive Wassermann and Kahn Reactions in Leprosy, Pub. Health Rep. **46**: 957 (April 24) 1931.
11. Faget, G. H., and Ross, H.: Evaluation of Positive Kolmer and Kahn Tests in Leprosy, Ven. Dis. Inform. **25**: 33 (May) 1944.
12. Faget, G. H.; Pogge, R. C.; Johansen, F. A.; Dinan, J. F.; Prejean, B. M., and Eccles, C. G.: The Promin Treatment of Leprosy: A Progress Report, Pub. Health Rep. **58**: 1729 (Nov. 26) 1943.

present study commenced. Of these patients there are 16 in whom the disease is arrested but who have elected to remain in the hospital or have returned after conditional release because of disabilities resulting from leprosy which prevent their gaining a livelihood and because they have no home to which to go nor the means to live elsewhere. That none of these patients have relapsed in spite of continuous exposure to infection can be interpreted as a hopeful sign that the disease can be eradicated, at least in some cases, and that it is possible thereafter for a permanent resistance to leprosy to be established.

SUMMARY

This report is based on data accumulated during the last fifteen years from 723 patients in the National Leprosarium. The Leprosarium does not continuously hospitalize any but citizens of the United States. The foreign born patients admitted are either naturalized citizens or subject to immigation regulations and deportation. Of the total number of patients 303 are foreign born and 420 native born. Of the foreign born more than 72 per cent are of Mexican, Philippine, British West Indies or Chinese nativity. Many of these probably had contracted the disease before their arrival in the United States and may have established foci which could account for the occurrence of some of the cases in native born citizens, especially in Texas, California and Florida.

From Texas the average yearly admissions are 12.2, nearly three times as many as formerly and greater than from any other state.

From Louisiana the average yearly admissions are 11.53, a little less than formerly but greater than from any other state except Texas. Formerly the admissions from Louisiana exceeded those from Texas.

From California and Florida there are enough admissions of native born to argue for an endemic origin, but there are also evidences of imported cases.

From New York and Illinois there are not enough natives of these states admitted to establish evidence of an endemic origin. Almost all cases are probably imported.

From Minnesota and Massachusetts the decline in admission warrants the belief that leprosy is not indigenous in those states and the foci established by immigration have disappeared or are rapidly disappearing.

Thirty-two Spanish-American War Veterans have been admitted, all of whom presumably contracted the disease in foreign countries in which leprosy is endemic.

Fifty-one veterans of World War I have been admitted who probably were infected before their induction into the Army.

Ten veterans of World War II have been admitted who were enlisted from endemic areas in the United States or were born in the Philippines, Mexico or Puerto Rico and presumably contracted the disease before their induction.

It is safe to predict from the experience of the Spanish-American War that a small number of those who serve in the armed forces in foreign countries where leprosy is prevelant will become its victims.

The average age on admittance is 35.5 years, and the greatest incidence is in the twenties and thirties.

The average age at onset of the disease is 30.4 years.

The duration of the disease before admission is from a few weeks to over forty years and averages five years.

The incidence in Louisiana of leprosy in the white race as estimated from admissions to the Leprosarium is twice that in the Negro race.

The proportion, including all races, of males to females is more than two to one.

There is not the usual proportion of two males to one female in the Negro race; there are approximately an equal number of Negro men and women.

The number of cases of the mixed type of leprosy almost equals the total of lepromatous and neural cases, and there are more lepromatous than neural cases.

There are 147 patients with a family history of leprosy, including 25 fathers, 24 mothers, 64 brothers, and 35 sisters and others less closely related.

The small number of cases in which there may have been marital transmission (only two couples) seems to indicate that contact is not the sole requisite for the transmission of leprosy.

No evidence is disclosed that any occupation is a predisposing cause. The employments of patients previous to admission are listed under one hundred and thirty different occupations, some of high and some of low rank in the social scale.

The first lesion is described as a macule by 259 patients and a nodule by 193. Both lesions occur primarily on regions that later are to be the sites of predilection for the eruption in the advanced stage of the disease. No probable port of entry is disclosed by the situations of the first lesions.

Other patients report sensory disturbances, of which anesthesia is the most common, as the earliest manifestations; a few recall blisters, painless burns and plantar ulcers, and some remember symptoms less characteristic of leprosy.

The usually employed serologic tests are of no value in the differentiation of leprosy from syphilis but are of value as an index of the prognosis and of the progress of leprosy.

During the period of study among the numerous experimental treatments investigated promin and diasone prove to be the most beneficial.

The average duration of life after the onset of leprosy is calculated as 10.3 years, but this average is derived from individual cases and is limited to a group of patients during a fifteen year period. In the tuberculoid type there is only one death eighteen years after the onset of leprosy. The duration from onset to death is longer in the neural cases than in either the lepromatous or the mixed cases.

Twenty per cent of the 723 patients admitted have been released conditionally as having the disease in arrested form and being no longer a menace to public health.

No patient with the tuberculoid type relapsed, but 9 per cent with the neural type, 12.5 per cent with the lepromatous type and 26 per cent with the mixed type relapsed.

In the table showing the causes of deaths it is seen that leprosy directly is responsible for only a small percentage of the deaths, while nephritis and tuberculosis are the direct cause of almost half of the fatalities.

"GAMMA GLOBULIN" AND "PLACENTAL GLOBULIN"

A COMPARISON OF THEIR EFFECTIVENESS IN THE PREVENTION AND MODIFICATION OF MEASLES

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Three agents are currently recommended for the prophylaxis of measles—convalescent human serum, placental globulin (immune globulin-human) and gamma globulin derived from normal human serum (human immune serum globulin). Concentrated, pooled ascites fluid [1] has also been suggested but has not come into general use and will not be discussed here. The prophylactic effectiveness of convalescent serum has been recently summarized in a well controlled study of 502 household contacts between the ages of 6 months and 15 years by Stillerman, Marks and Thalhimer.[2] These authors obtained complete protection in 50 per cent, modified measles in 49 per cent and regular measles in 1 per cent of the individuals studied. While the effectiveness of convalescent serum is not questioned, its lack of ready availability and the comparatively large doses which are necessary make its use unpractical. This study is directed toward the comparison of the effectiveness and incidence of untoward reactions of the remaining two agents—placental globulin (immune globulin-human) and normal human serum gamma globulin (human immune serum globulin). The characterization of normal human serum gamma globulin (human immune serum globulin) has been published by Cohn and his co-workers.[3] This material will be referred to hereafter in this paper as gamma globulin. Placental globulin (immune globulin-human) will hereafter be referred to as placental globulin.

In evaluating the literature on the prophylaxis of measles, those studies in which household contacts were used are the most significant. The smaller number of secondary cases occurring following the casual exposure of contacts in hospitals, schools or playgrounds, compared with the larger number occurring among those intimately exposed in the home, has been pointed out by a number of observers [4] and has been particularly stressed by Karelitz and Schick.[5] The latter authors also pointed out that the contact is more intimate in the homes of the poor than in the homes of the well-to-do.

The use of immune globulin obtained from human placentas in the prophylaxis of measles was first introduced by McKhann and Chu [6] in 1933. In one of his later papers McKhann [7] analyzed a group of 2,704 contacts in whom the exposure was both casual and intimate. Two groups of contacts were said to be intimately exposed, but no statement was made indicating place of exposure. One of these groups, totaling 585 cases, was given placental globulin for protection, the other group of 1,263 cases for modification. The exact doses and time of injections were not given, but it would appear from the text that in the latter group the doses, ordinarily effective for prevention when given early in the incubation period, were injected on the eighth day following initial exposure to obtain modification. When the results of the two groups were combined, there was obtained complete protection in 48.5 per cent, modification in 44.4 per cent and failure in 7 per cent. Reactions occurred in somewhat less than half the cases and were severe in approximately 5 per cent. Karelitz, Greenwald and Klein [8] treated 64 contacts exposed in homes with good hygiene with 10 to 20 cc. of placental globulin on the second to fifth day of exposure. Protection was obtained in 40 per cent, modification in 48 per cent and failure in 12 per cent. Among the 64 cases there were 34 severe reactions, of which 8 were general and 26 local. In a study conducted by the Chicago Department of Health [9] a group of 678 household contacts under the age of 10 were treated with placental globulin in doses of 2 to 3.35 cc. Complete protection was obtained in 52.1 per cent, modification in 43.2 per cent and failure in 4.7 per cent. More than 60 per cent of the children injected were under 1 year of age in whom there would still be some inherited passive immunity. Bloxsom [10] reported the results in private practice of a study of 107 children, most of whom were between the ages of 1 and 8, who were exposed either in their homes or in the bus going to and from school and who were injected with 2 cc. of placental globulin during the period from the fifth to the ninth day after exposure. Measles developed in 31.8 per cent, among whom it was mild in 68 per cent, moderate in 29 per cent and severe in 3 per cent. Reactions occurred in 95 per cent of the total group, 81 per cent of which were mild and 14 per cent severe.

Two reports on the prophylactic use in measles of gamma globulin have appeared. Stokes, Maris and

Dr. William Thalhimer put his experience at our disposal and gave valuable aid in planning the investigation.

From the Bureau of Preventable Diseases and the Bureau of Laboratories, Department of Health, City of New York.

The physicians of the Bureau of Preventable Diseases of the New York City Department of Health performed the field work in this study and followed up the contacts.

The American National Red Cross cooperated in this study in order to determine the effectiveness of gamma globulin in the prophylaxis of measles on a community basis.

The products of plasma fractionation employed in this work were developed from blood collected by the American Red Cross, by the Department of Physical Chemistry, Harvard Medical School, Boston, under a contract recommended by the Committee of Medical Research between the Office of Scientific Research and Development and Harvard University. Dr. Edwin J. Cohn and Dr. J. L. Oncley of the Department of Physical Chemistry and Dr. Charles A. Janeway of the Department of Pediatrics of Harvard Medical School gave their cooperation.

1. Thalhimer, W., and Stillerman, M.: Prevention and Modification of Measles with Concentrated Pooled Ascites Fluid and with Its Globulin Fraction, Proc. Soc. Exper. Biol. & Med. **42:** 683-687 (Dec.) 1939.

2. Stillerman, M.; Marks, H. H., and Thalhimer, W.: Prophylaxis of Measles with Convalescent Serum, Am. J. Dis. Child. **67:** 1-14 (Jan.) 1944.

3. Cohn, E. J.; Oncley, J. L.; Strong, L. E.; Hughes, W. L., Jr., and Armstrong, S. H., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: I. The Characterization of the Protein Fractions of Human Plasma, J. Clin. Investigation **23:** 417-432 (July) 1944.

4. Park, W. H., and Freeman, R. G., Jr.: The Prophylactic Use of Measles Convalescent Serum, J. A. M. A. **87:** 556-558 (Aug. 21) 1926. Levinson, S. O.; McDougall, C., and Thalhimer, W.: Use of Convalescent Serum for the Prevention and Attenuation of Measles, Illinois M. J. **63:** 258-265 (March) 1933. McKhann, C. F.; Green, A. A., and Coady, H.: Factors Influencing the Effectiveness of Placental Extract in the Prevention and Modification of Measles, J. Pediat. **6:** 603-614 (May) 1935. Eley, R. C.: Placental Extract (Immune Globulin-Human) with Special Reference to Its Use in Prevention and Modification of Measles, J. Michigan M. Soc. **35:** 769-772 (Dec.) 1936.

5. Karelitz, S., and Schick, B.: Epidemiologic Factors in Measles Prophylaxis, J. A. M. A. **104:** 991-994 (March 23) 1935.

6. McKhann, C. F., and Chu, F. T.: Antibodies in Placental Extracts, J. Infect. Dis. **52:** 268-277 (March-April) 1933.

7. McKhann, C. F. The Prevention and Modification of Measles, J. A. M. A. **109:** 2034-2038 (Dec. 18) 1937.

8. Karelitz, S.; Greenwald, C. K., and Klein, A. J.: Placental Fluid in Measles Prophylaxis, J. Pediat. **10:** 170-174 (Feb.) 1937.

9. Bundesen, H. N.; Fishbein, W. I.; Abrams, I. R., and Miller, R. D.: Clinical Use of Immune Human Placental Globulin in Chicago, J. A. M. A. **115:** 104-107 (July 13) 1940.

10. Bloxsom, A.: Clinical Evaluation of the Use of Immune Human Placental Globulin in Attenuation of Measles, Texas State J. Med. **37:** 302-304 (Aug.) 1941.

Gellis [11] reported the results of prophylaxis with gamma globulin in 891 household contacts of all ages in the private practice of a number of physicians. They obtained 71.4 per cent protection and 28.6 per cent modification, using doses between 0.5 and 5.0 cc. Ordman, Jennings and Janeway [12] used a dose of 2 cc. for infants between the ages of 6 months and 1 year, 2.5 cc. for children between 1 and 5 years and 5 cc. for children over 5 years of age. In 139 household contacts among underprivileged families in Boston they obtained complete protection in 71 per cent, modification in 27 per cent and typical measles in 2 per cent.

PLAN OF STUDY

Gamma globulin and placental globulin were studied under the same conditions in household contacts of similar age distribution (table 1) and at similar periods following exposure to the source case (table 2). The contacts were all in the age group from 6 months through 6 years, most of whom were between the ages of 6 months through 3 years (table 1). All contacts were known not to have had measles previously, and therefore all contacts referred to in this study are considered to be susceptible contacts.

All contacts were seen by physicians trained in the diagnosis of acute communicable disease on the staff of the New York City Department of Health. Private physicians reporting cases of measles were interviewed by one of these physicians, questioned about the number and ages of household contacts and an offer of gamma globulin or placental globulin for passive immunization of contacts was then made to them. They were advised that the injections of the material might be given by them or if they preferred by physicians of the department of health. The offer was conditioned by permission from the private physician to the physician of the department of health to visit and examine the source case and to make follow-up visits to the contacts for a period of twenty-one days following the first exposure. Where there was no physician in attendance, the offer was made directly to the parents. As soon as a case of measles was reported and the offer of immunization of contacts was accepted by the physician or parents, the physician of the department of health visited the home, examined the source case and completed a form on which were listed the name, age, sex and home address of the patient, as well as the presence or absence of coryza, conjunctivitis, rash (with date of onset), Koplik spots and fever. In addition there were listed the names and ages of all household contacts, and a note was made on the degree and adequacy of isolation of the case. If the diagnosis of a primary case was confirmed, the gamma globulin or placental globulin was injected subcutaneously into the contacts or, where arrangements had been previously made, the material was left at the home for injection that day by the private physician. A separate form was then made out for each household contact injected on which were listed the name, age, address, sex and relationship of the contact, the nature, the lot number and amount of material used, the date of injection, the symptoms of measles, if any, and the date of appearance of the rash in the source case.

In 49 per cent of homes economic conditions were such that no attempt could be made to carry out any sort of isolation in the primary case. Furthermore, all children with primary measles remained at home, so that there were frequent opportunities for contact between them and the other children of the family. Since diagnosis was rarely made before the appearance of the rash, which is considered in this study to be the fourth day of illness, there was continuous contact between the patient and the contacts for at least four days of the period of greatest communicability even in those homes where attempts were made to isolate the contacts after the diagnosis had been made. All the contacts studied were exposed to cases in the same household. Those contacts living in the same house but not in the same household as the source case were excluded.

TABLE 1.—*Percentage Distribution of Children Injected with Gamma Globulin and with Placental Globulin by Age*

Age	Gamma Cases	Globulin, per Cent	Placental Cases	Globulin, per Cent
6-9 months	86	10.6	9	10.0
9-12 months	84	10.1	7	7.8
1 year	236	29.0	25	27.8
2 years	169	20.7	14	15.6
3 years	129	16.0	19	21.1
4 years	61	7.4	10	11.1
5 years	41	5.0	4	4.4
6 years	8	1.1	2	2.2
Totals	814	100.0	90	100.0

TABLE 2.—*Percentage Distribution of Children Injected with Gamma Globulin and with Placental Globulin by Day of Exposure on Which Injection Was Made*

Day of Exposure Injected	Gamma Cases	Globulin, per Cent	Placental Cases	Globulin, per Cent
1	0	...	0	...
2	2	0.2	2	2.2
3	13	1.6	2	2.2
4	172	20.7	21	23.3
5	296	36.7	35	38.8
6	203	24.8	19	21.1
7	81	9.8	5	5.5
8	29	3.6	3	3.3
9	8	1.0	2	2.2
10	10	1.2	1	1.1
Totals	814	100.0	90	100.0

Follow-up visits were made by the physicians of the department of health two days after the appearance of the rash in the source case to rule out primary measles in the contact. The next visit was made seven days after the appearance of the rash in the source case and thereafter visits were made every other day until the seventeenth day after the appearance of the rash in the source case. Since the rash usually occurs on the fourth day after onset of symptoms, it was considered that the contacts were followed for twenty-one days after the onset of the disease in the source case. If no measles developed by that time, the follow-up was terminated and the contact was considered to have been completely protected. If measles developed in a contact, the physician revisited once or twice to determine the degree of severity of symptoms and to complete the form. The date of onset of measles in the contact was noted and the severity of measles was evaluated (modified from the classification of Stillerman, Marks and Thalhimer,[2]) on the basis of the severity of four symptoms: (1) coryza and conjunctivitis, (2) cough, (3) fever and (4) rash. Each of these symptoms was divided into three categories, A, B and C. For coryza and conjunctivitis, A represented mild,

11. Stokes, J., Jr.; Maris, E. P., and Gellis, S. S.: Chemical, Clinical and Immunological Studies on the Products of Plasma Fractionation: XI. The Use of Concentrated Normal Human Serum Gamma Globulin (Human Immune Serum Globulin) in the Prophylaxis and Treatment of Measles, J. Clin. Investigation **23**: 531-540 (July) 1944.

12. Ordman, C. W.; Jennings, C. G., and Janeway, C. A.: Chemical, Clinical and Immunological Studies on the Products of Plasma Fractionation. XII. The Use of Concentrated Normal Human Serum Gamma Globulin (Human Immune Serum Globulin) in the Prevention and Attenuation of Measles, J. Clin. Investigation **23**: 541-549 (July) 1944.

B moderate and C severe redness and discharge. For cough, A indicated occasional, B moderate and C frequent cough. For fever, A represented a temperature of 99 to 101 F., B 101 to 102.5 F. and C 102.5 F. and higher. For the rash, A signified occasional lesion, B a moderate number of scattered spots and C a generalized rash. To obtain a quantitative value for mild, moderate and severe measles, all A's were given a numerical value of 1, all B's a value of 2 and all C's a value of 3. The disease was considered mild if the sum of the values did not exceed 6, moderate if the sum was 7 or 8 and severe if the sum was 9 or over.

In the cases of gamma globulin the material in solution at a concentration of twenty-five times that of pooled adult serum from which it was derived was rebottled in the Bureau of Laboratories of the New York City Department of Health so that each vial contained 2 cc.[13] The dose for each case was the total contents of the vial. The same dose was used for all contacts regardless of age (6 months through 6 years). In the case of placental globulin the material was distributed in 5 cc. vials[14] and the total contents of the vial were injected into each contact. A total of 814 household contacts were injected with gamma globulin and 90 contacts were injected with placental globulin.[15]

TABLE 3.—*Comparison of Gamma Globulin and Placental Globulin in Prophylaxis of Measles in Household Contacts*

Material Used	Number Injected	No Measles		Mild Measles		Moderate Measles		Severe Measles	
		No.	%	No.	%	No.	%	No.	%
Gamma globulin	814	641	78.7	160	19.7	13	1.6	0	0
Placental globulin	90	35	38.9	24	26.6	10	11.1	21	23.3

RESULTS OF THE STUDY

Among the 814 contacts injected with 2 cc. of gamma globulin 641, or 78.7 per cent, did not develop measles, 160, or 19.7 per cent, developed mild measles and 13, or 1.6 per cent, developed moderate measles. None developed severe measles. In contrast, among 90 receiving 5 cc. of placental globulin 35, or 38.9 per cent, did not develop measles, 24, or 26.6 per cent, developed mild measles, 10, or 11.1 per cent, developed moderate measles, and 21, or 23.3 per cent, developed severe measles (table 3). It will be noted that the results obtained with gamma globulin are significantly better than those obtained by the use of placental globulin.

Among the 814 contacts injected with gamma globulin, reactions occurred in 7, or less than 1 per cent of the group. Two of the reactions were general, consisting of fever which rose on the day following injection to 104 F. in one and to 100 F. in the other. The five local reactions consisted of slight induration about the site of the injection, which lasted a few hours. In contrast, among the 90 cases in which placental globulin was administered, reactions occurred in 37, or 41 per cent. There were 18 general reactions, 10 of these consisting of anorexia, restlessness and sleeplessness and 8 with the aforementioned symptoms plus fever, under 101 degrees F. in 3 and over 103 F. in 5. Local reactions occurred in 23 and consisted of pain, swelling, redness and induration about the site of the injection, lasting from one to two days.

TABLE 4.—*Results of Immunization with 2 Cc. of Gamma Globulin by Age*

Age	Number Injected	No Measles		Mild Measles		Moderate Measles	
		No.	%	No.	%	No.	%
6-9 months	86	84	97.6	2	2.3	0	0.0
9-12 months	84	77	91.7	6	7.1	1	1.1
1 year	236	189	80.0	44	18.6	3	1.3
2 years	169	132	78.1	35	20.7	2	1.2
3 years	129	92	71.3	35	27.1	2	1.6
4 years	61	39	64.0	19	31.1	3	4.9
5 years	41	25	61.0	15	36.5	1	2.4
6 years	8	3	37.5	4	50.0	1	12.5
Total	814	641	78.7	160	19.7	13	1.6

The result of the immunization of gamma globulin was analyzed by age (table 4). It will be noted that the older the child, the less the degree of complete protection. The high degree of complete protection obtained by infants under 1 year of age probably represents a combination of passive immunization acquired from the mother and passive immunization artificially conferred by the gamma globulin. The drop in protection in the older children might be explained by the fact that a constant dose of gamma globulin was given regardless of body weight. This is probably a desirable situation, since the experimental dosage attempted in this study conferred complete protection on infants and small children and tended toward modification in the case of the older children.

It is of interest to compare these results with an additional 38 similar contacts with similar age distribution who were injected with 1 cc. of gamma globulin. In this group 20, or 52.6 per cent, were completely protected, 11, or 28.9 per cent, developed mild measles, 6, or 15.8 per cent, developed moderate measles and 1, or 2.7 per cent, developed severe measles.

TABLE 5.—*Results of Immunization with 2 Cc. of Gamma Globulin by Day of Exposure on Which Injection Was Made*

Day of Exposure on Which Injection Was Made	Number Injected	No Measles		Mild Measles		Moderate Measles	
		No.	%	No.	%	No.	%
1st	0	0	0.0	0	0.0	0	0.0
2d	2	1	50.0	1	50.0	0	0.0
3d	13	10	76.9	3	23.1	0	0.0
4th	172	136	79.0	33	19.1	3	1.7
5th	296	232	78.3	61	20.6	3	1.0
6th	203	170	83.7	31	15.2	2	0.9
7th	81	60	71.6	19	23.4	2	2.4
8th	29	22	75.9	5	17.2	2	6.9
9th	8	3	37.5	5	62.5	0	0.0
10th	10	7	70.0	2	20.0	1	10.0
Total	814	641	78.7	160	19.7	13	1.6

In table 5 the results of immunization of the 814 contacts given gamma globulin were analyzed by day of injection following first exposure to measles. If those injected on the second, ninth and tenth days are excluded from consideration because of the small number of cases in those categories, it will be noted that there is no significant difference in the amount of complete protection obtained after the injection of gamma globulin from the third to the eighth day following initial exposure.

13. The vials actually contained 2.2 cc. to allow for loss on withdrawal of material from the vial.

14. The placental globulin in part was obtained from a commercial source and in part from a noncommercial source.

15. This experiment was performed in part (171 injected contacts) with five experimental lots of gamma globulin, each of which was prepared in a slightly different manner from that of the standard lots. In four of these experimental lots (147 injected contacts) results were similar to those obtained with standard lots and are included in the report. One of these lots (S 1-1) produced results quite different from that of the remaining lots and those results are not included in the tabulation. The results obtained with this lot are as follows: 24 contacts were injected, 16 did not develop measles, 4 developed mild measles, 1 moderate measles and 3 severe measles.

In evaluating the results obtained by prophylactic materials, it is necessary to know the secondary attack rate of household contacts to cases when no immunizing procedures are used. The rate in measles has been shown to be fairly uniform in different communities, particularly for ages under 14. Stillerman and Thalhimer [16] have listed the secondary attack rate of regular measles among susceptible contacts as reported in the literature and have added rates of their own. From their table we have calculated the secondary attack rates for children up to the age of 7, from the figures of Chapin in Providence, R. I., 88 per cent (1917-1923), Wilson in Providence, R. I., 88 per cent (1929-1934), Fales in Baltimore, 82 per cent (1936-1937), Top in Detroit, 80 per cent (1935) and Butler in Wilesden, England, 84 per cent (1908-1911). In the age group under 7 Stillerman and Thalhimer obtained a rate of 78 per cent in New York City.

In this study all family contacts from 6 months through 6 years of age whose physician or parents refused to have them inoculated were followed in the same fashion by the same personnel as the contacts receiving prophylaxis. Among 65 such contacts 54 developed measles, an attack rate of 83 per cent, which is similar to the secondary attack rates as calculated from the summaries of Stillerman and Thalhimer.[16] Among those 54 cases the measles was mild in 11, or 20 per cent, moderate in 12, or 22 per cent, and severe in 31, or 57 per cent. It is evident that the results obtained in this study, particularly with the use of gamma globulin, are strikingly different from the secondary attack rates of measles in this age group when no prophylactic agent is used.

COMPARISON OF THE PHYSICOCHEMICAL AND IMMUNOLOGIC CHARACTERISTICS OF GAMMA GLOBULIN AND PLACENTAL GLOBULIN [17]

In table 6 [18] it is evident that the concentration and total amount of gamma globulin and the titers of the various immunologic tests performed show that the lots of gamma globulin used in the study had a consistently higher potency than the lot of placental globulin tested. Since there is no laboratory method for determining the concentration of measles antibody, it is not possible to make a direct comparison between the clinical results obtained in this study and the laboratory studies of the materials. However, since the concentration and the amount of gamma globulin and the concentration of all the other antibodies studied are consistently less in the placental globulin, the concentration of measles antibody might also be expected to be less in the placental globulin.

COMMENT

The morbidity of measles has not declined over the years, as has that of diphtheria. In New York City in 1941 there were 80,000 cases reported, more cases than in any previous year. Although there has been a decline in mortality, deaths still occur. For the five year period 1939-1943 there were 49 deaths in New York City, 80 per cent of which occurred in the first five years of life. These statistics suggest that, in the absence of an effective active immunizing agent, passive prophylaxis should be administered to household contacts during the first five years of life.

Since convalescent serum is not generally available, and the dosage required is large, the results of this study would indicate that gamma globulin is the agent of choice in the prophylaxis of measles. Gamma globulin can be produced in large quantities, it confers adequate protection in small doses and the number of untoward reactions is minimal. Further studies are needed to determine the minimal protective or modifying dose in each age group.

SUMMARY AND CONCLUSIONS

1. Gamma globulin was administered in a uniform dose of 2 cc. to 814 household contacts (between the ages of 6 months through 6 years) of cases of measles. None developed regular measles, 78.7 per cent were completely protected and 21.3 per cent had modified measles. Among those cases of modified measles, 92 per cent were mild measles and 8 per cent moderate measles. There was a tendency for the effectiveness to decrease with age, but the amount of complete protection was not affected by the day of exposure on which the injection was made from the third to the eighth day following initial exposure to the original case. Untoward reactions were rare.

TABLE 6.—*Comparison of Chemical and Immunologic Determinations on the Lots of Gamma Globulin and Placental Globulin Used in This Study*

Measurement	Gamma Globulin, Range of Lots †	Placental Globulin ‡
Chemical		
Protein concentration, Gm./100 cc.	15.3-22.4	4.4
Electrophoretic analysis:		
Albumin and		
Alpha globulin, per cent	0-4	29
Beta globulin, per cent	0-14	38
Gamma globulin, per cent	85-99	33
Immunologic *		
Diphtheria antitoxin	0.4-1.1	0.024
Influenza A		
Complement fixation	0.7-4.0	<0.04
Hirst test	0.5-2.0	0.06
Mouse protection	0.8-1.7	0.033
Mumps complement fixation	0.7-1.4	<0.04
Typhoid		
H agglutinin	0.2-2.0	0.02
O agglutinin	0.5-1.0	0.5
Streptococcus antitoxin	0.5-1.1	Not done

* Immunologic measurements are expressed as a ratio of the titer of the solution to the titer of reference lot IIG-66 of human immune serum globulin,[18] the value for lot IIG-66 being considered as one.

† Data on human immune serum globulin is presented in terms of the range of determinations in the various lots used (lots IIG-84, 11GS-74B, IIG1-120, IIG2-L371, S 1, S 4 and U 8214-2).

‡ Lot number 41 (Immune Globulin-Human).

2. Placental globulin was injected into 90 similar contacts in a dose of 5 cc. Severe measles occurred in 23.3 per cent, 38.9 per cent were completely protected and 37.7 per cent had modified measles. Among the cases of modified measles 70 per cent were mild and 30 per cent were moderate. Reactions occurred in 41 per cent of those injected.

3. In a group of 65 contacts of similar age distribution who received no prophylaxis 54, or 83 per cent, developed measles. Of these 31 per cent were severe, 12 moderate and 10 mild. This experience is consistent with that of similar groups reported elsewhere.

4. Physicochemical and immunologic studies of gamma globulin and placental globulin demonstrated that gamma globulin is the more potent of the two agents.

5. Gamma globulin (human immune serum globulin) is the material of choice in the prophylaxis of measles.

16. Stillerman, M., and Thalhimer, W.: Attack Rate and Incubation Period of Measles, Am. J. Dis. Child. **67**: 15-21 (Jan.) 1944.

17. Dr. J. W. Williams of the Department of Chemistry of the University of Wisconsin, Dr. J. L. Oncley of the Department of Physical Chemistry, Harvard Medical School, made the chemical studies, and Dr. J. F. Enders of the Department of Bacteriology, Harvard Medical School, made the immunologic studies on these materials. Dr. Williams worked under contract OEMcmr-142 and Dr. Oncley and Dr. Enders under contract OEMcmr-139, recommended by the Committee on Medical Research.

18. Enders, J. F.: Chemical, Clinical and Immunological Studies on the Products of Plasma Fractionation: X. The Concentrations of Certain Antibodies in Globulin Fractions Derived from Human Blood Plasma, J. Clin. Investigation **23**: 510-530 (July) 1944.

TREATMENT OF HUMAN ANTHRAX WITH PENICILLIN

REPORT OF THREE CASES

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Human anthrax, although not a widespread disease, continues to be an important medical problem among workers in the wool and leather industries. The introduction of more rational and effective methods of prophylaxis and treatment have lowered the incidence and death rate in anthrax but the disease continues to carry a significant mortality. In the five year period 1938 to 1942, exclusive of West Virginia, there were 390 cases of human anthrax reported in the United States, with a mortality rate of 13.8 per cent, which compares favorably with a mortality rate of 15.1 per cent during the period 1933 to 1937 and which represents a distinct advance over the period 1928 to 1932, when among 394 reported cases 106, or 26.8 per cent, ended fatally.[1]

The epidemiology and prophylaxis of anthrax, which are important problems in industrial hygiene, are discussed in great detail in the report of the symposium on anthrax[2] held by the Department of Health of the State of Pennsylvania in 1941. Suffice it to say here that great strides have been made in attempting to reduce the incidence of this disease in industry.

There is still not full agreement among authorities as to the treatment of choice in human anthrax. In 1941 Lucchesi and Gildersleeve[3] in a report on the treatment of 67 patients at the Philadelphia Hospital for Contagious Diseases concluded that the administration of neoarsphenamine is the method of choice in most cases but that serum is the preferred agent when (1) the lesion is on the face or neck, (2) the blood stream has been invaded and (3) the patient has the "internal" type of anthrax. Furthermore, these authors felt that some patients with cutaneous anthrax "will get well without treatment if the lesion is left alone." Gold,[4] reporting on the treatment of 60 cases of human anthrax, states that "sulfonamide compounds are a safe and reliable substitute for antianthrax serum" but presents several cases in which the sulfonamides appeared ineffective and serum was required for recovery. All authorities agree that attempts at destruction or removal of the lesion are fraught with grave danger and are strictly contraindicated.

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The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council. The work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania. This paper was prepared for publication in March 1944 but not released by the Committee on Medical Research until September 26, 1944.

1. Communication from the United States Public Health Service, January 1944.

2. Symposium on Anthrax, Department of Health, Commonwealth of Pennsylvania, Harrisburg, 1941.

3. Lucchesi, P. F., and Gildersleeve, N.: The Treatment of Anthrax, J. A. M. A. **116:** 1506 (April 5) 1941.

4. Gold, H.: Anthrax: A Review of Sixty Cases, with a Report on the Therapeutic Use of Sulfonamide Compounds, Arch. Int. Med. **70:** 785 (Nov.) 1942.

In his epoch making paper in 1929, announcing the discovery of penicillin, Dr. Alexander Fleming[5] observed that the growth of Bacillus anthracis was inhibited in vitro by a penicillin concentration of 1:10. This compared with the inhibition of Staphylococcus aureus at a concentration of 1:400 and lack of inhibition of some gram negative bacilli at a concentration of 1:5. Abraham and his collaborators[6] found that the growth of one strain of B. anthracis was inhibited in vitro at the same concentration as that which inhibited four different strains of Staphylococcus aureus. It seemed, therefore, that penicillin might be effective in the treatment of human anthrax. The 3 cases reported here are all of the nonbacteremic, cutaneous type and were proved bacteriologically. They were consecutive and unselected, and penicillin was the only specific medication administered.

REPORT OF CASES

Case 1.—*History.*—S. G., a white woman aged 34, a wool worker, first noticed a whitish "pimple" on her left forearm on Oct. 29, 1943. The lesion increased in size, became painful and on November 1, the third day of the disease, she was admitted to the Philadelphia Hospital for Contagious Diseases. On admission the temperature was 99 F., the pulse rate was 102 and the patient appeared slightly toxic and anxious. The lesion, which was on the flexor surface of the left forearm 9 cm. from the wrist, measured about 2 cm. in diameter and consisted of a central black eschar surrounded by a zone of small vesicles. Almost the entire flexor surface of the forearm from the wrist to the antecubital space was indurated and erythematous. The history and physical examination were otherwise noncontributory.

A continuous intravenous infusion containing penicillin was started on admission and continued for five hours, at which time, owing to technical difficulties, the infusion was stopped, so that the patient received approximately 25,000 units initially. Examination of the lesion at this time revealed that the area of erythema and induration about the lesion had almost completely disappeared. The intravenous infusion was then restarted and continued for twenty-four hours, during which time the patient received an additional 150,000 units of penicillin. The intramuscular route was then used and the patient received 12,500 units intramuscularly every two hours for forty-eight hours. The course of therapy lasted a little over three days and the patient received a total of 475,000 units of penicillin, of which 175,000 was given intravenously and 300,000 units intramuscularly.

The temperature remained normal after eighteen hours of therapy, the pain disappeared almost immediately and examination four days after admission showed that the erythema and induration had disappeared while the vesicles had become dry. The patient was discharged in good condition on the ninth hospital day.

Laboratory Studies.—Blood examination revealed hemoglobin 12 to 13 Gm. and white blood cells 6,400 to 8,400, with 68 per cent neutrophils, 20 per cent lymphocytes and 11 per cent monocytes. Kolmer and Kahn tests were negative. Blood culture on admission was negative. Culture of the local lesion on admission and before penicillin was started was positive for B. anthracis. Cultures taken on the third, seventh and eighth days after admission were negative.

Case 2.—*History.*—D. S., a Negro woman aged 18, a wool worker, was admitted to the Philadelphia Hospital for Contagious Diseases on Nov. 20, 1943, four days after she had

5. Fleming, A.: The Antibacterial Action of Cultures of a Penicillium with Special Reference to Their Use in the Isolation of B. Influenzae, Brit. J. Exper. Path. **10:** 226 (June) 1929.

6. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. C.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, Lancet **2:** 177 (Aug. 16) 1941.

first noticed a small papule on the left side of her face. This papule had increased in size so that on admission to the hospital examination revealed a circular lesion on the left side of the face above the zygoma measuring 2 cm. in diameter. It consisted of a central black eschar covered with a serosanguineous discharge and surrounded by small clusters of vesicles. Just peripheral to the lesion was an area of erythema and induration measuring 2 cm. in width. An enlarged and tender left preauricular lymph node was palpable. The temperature was 99.4 F. The history and physical examination were otherwise negative.

A continuous intravenous infusion of penicillin was begun, and during the first fifty-three hours the patient received 225,000 units in this manner. Then, because of the development of a mild thrombophlebitis, a change to the intramuscular route was made and the patient received injections of 8,333 units every two hours for twenty-four hours. The course of penicillin therapy lasted a little over three days and the patient received a total of 325,000 units, of which 225,000 units was given intravenously and 100,000 units intramuscularly.

Twelve hours after the onset of therapy the erythema was less, the serous discharge had disappeared, the vesicles had become dry and the preauricular lymph node was no longer tender. At the end of seventy-two hours of treatment all edema and erythema had disappeared, and the lesion was quite dry and appeared innocuous. The thrombophlebitis resulting from the intravenous infusion cleared up rapidly under conservative measures and the patient left the hospital on the ninth hospital day.

Laboratory Studies.—Hemoglobin was 77 to 87 per cent; white blood cells numbered 11,900 to 8,200, with 63 per cent neutrophils, 35 per cent lymphocytes and 2 per cent monocytes; Kolmer and Kahn tests were negative. Blood culture on admission was negative. Smear and culture of the local lesion were positive for B. anthracis on admission (before the administration of penicillin) and on the day following admission (after about 50,000 units of penicillin had been administered). Cultures and smears taken on the second, third, fourth, eighth and ninth days after admission were negative.

CASE 3.—*History.*—L. D., a white woman aged 34, a wool worker, on Dec. 10, 1943 noticed a small "pimple" on the ulnar aspect of her left forearm. On December 14 she received 0.3 cc. of staphylococcus vaccine. A smear of the lesion made on the following day showed B. anthracis, and she was admitted to the Philadelphia Hospital for Contagious Diseases on December 15, five days after the onset of the disease.

Physical examination revealed a temperature of 99.8 F. and a normal pulse, respiratory rate and blood pressure. On the ulnar aspect of her left forearm just above the wrist was a round, purplish red, partially crusted, oozing lesion measuring 2 cm. in diameter. Just peripheral to the lesion were a few clusters of vesicles, and the entire lesion was surrounded by a zone of erythema and induration. There was no adenopathy, and the history and physical examination were otherwise negative.

A continuous intravenous infusion of penicillin was started and continued for forty-eight hours, so that she received a total of 100,000 units intravenously at the rate of 50,000 units per day.

After she had received about 40,000 units, examination revealed that the erythema and induration about the lesion had decreased considerably. After 100,000 units had been administered the lesion looked dry and the erythema had completely disappeared. The patient was discharged on the tenth hospital day.

Laboratory Studies.—Hemoglobin was 80 per cent; white blood cells numbered 9,200 to 7,600, with 72 per cent neutrophils, 20 per cent lymphocytes and 8 per cent monocytes. Kolmer and Kahn tests were negative. Blood culture on admission was negative. Smear and culture of the local lesion on admission were positive for B. anthracis. Smear and culture taken on the first and second days after admission were also positive. Smear taken on the third day, after the administration of 100,000 units of penicillin, showed a few organisms but the culture was negative. The same was true on the fourth day. On the fifth, sixth, seventh, tenth and eleventh days after admission both smear and culture were negative.

COMMENT

The clinical response of these cases of anthrax to penicillin was rapid and definite. In each instance the inflammatory reaction about the lesion showed very prompt regression and the lesion itself underwent rapid involution.

The clinical response was paralleled by the disappearance of B. anthracis from the lesion. The organism in case 1 could not be seen or cultured after the administration of 475,000 units of penicillin. In case 2 culture and smear were positive after 50,000 units of penicillin had been given but were negative after the administration of 150,000 units. A small dosage of penicillin was deliberately given in case 3, and here it was seen that after 50,000 units culture and smear were still positive. After 100,000 units the smear remained positive but showed few organisms, and the culture was negative. Twenty-four hours after the administration of 100,000 units of penicillin the smear was still positive and culture was negative, but in forty-eight hours both smear and culture were negative. In none of the 3 cases did the organism reappear in smear or culture after its initial disappearance.

Comparative Susceptibility of B. Anthracis to Penicillin

Concentration of Penicillin in Culture Medium, Units per Cc.	Organism		
	Staphylococcus Aureus	B. Anthracis	E. Coli
0.01	++	++++	++++
0.025	0	++++	++++
0.05	0	++++	++++
0.1	0	++++	++++
0.25	0	+++	++++
0.5	0	++	++++
1.0	0	+	++++
2.5	0	0	++++
5.0	0	0	++++
10.0	0	0	++++

++++ indicates luxuriant growth; +++, moderate growth; ++, slight growth; +, very slight growth; 0, no growth.

On the basis of these bacteriologic and clinical data it would seem that a total of 100,000 units of penicillin is certainly the minimum effective dose in the uncomplicated case of cutaneous anthrax. At least a total of 200,000 to 400,000 units of penicillin, given at the rate of 100,000 units in twenty-four hours, should be administered to the average adult, and this amount should effect a prompt and satisfactory therapeutic response. Continuous intravenous infusion is probably the most efficient route of administration, although intramuscular injections every two to three hours might be just as effective. No case of visceral anthrax or severe cutaneous anthrax with bacteremia has been treated with penicillin to our knowledge. In these cases larger doses should undoubtedly be administered by the intravenous route and perhaps serum should be given in addition.

The strain of B. anthracis isolated in case 3 was tested in vitro for its sensitivity to penicillin by Miss Marjorie Wiley and was compared to Staphylococcus aureus and Escherichia coli. As may be seen in the table, the growth of B. anthracis was completely inhibited by a concentration of 2.5 units of penicillin per cubic centimeter; the growth of Staphylococcus aureus was completely inhibited by a concentration of 0.025 unit per cubic centimeter, but the growth of E. coli remained uninhibited in all concentrations. In other words, this strain of B. anthracis, although sensitive to penicillin, was one hundred times less sensitive than Staphylococcus aureus. Fleming's strain [5] was forty times less sensitive than Staphylococcus aureus, while the organism of Abraham and his collaborators [6] appeared to possess the same sensitivity as Staphylococcus aureus. Allowing for possible differences in the resistance of the various strains of Staphylococcus aureus used in each study, it nevertheless appears likely that different strains of B. anthracis may vary widely in their sensitivity to penicillin in vitro. This study also suggests that one must exercise some caution in predicting the clinical response of a disease to penicillin therapy on the basis of in vitro response of the etiologic agent to penicillin, for in this instance we have an example of a disease which shows pronounced clinical response to the administration of penicillin in small dosage and yet is caused by an organism which has been observed to possess a relatively low sensitivity to penicillin in vitro.

The place of penicillin in the therapy of anthrax and its relation to the other agents already used in this disease cannot be finally determined on the basis of 3 cases. Suffice it to say that penicillin is a chemotherapeutic agent of low toxicity which, in relatively small doses, appears to be remarkably effective in the treatment of cutaneous human anthrax. We believe that penicillin will acquire a prominent place in the treatment of this disease and that further clinical trial is warranted.

SUMMARY AND CONCLUSIONS

1. Three cases of uncomplicated cutaneous human anthrax without bacteremia were treated with penicillin. As far as we know, this is the first report on the use of penicillin in the treatment of patients with cutaneous anthrax.

2. Exceedingly prompt and excellent clinical response to penicillin was observed in every case.

3. Bacteriologic studies showed that there was rapid disappearance of B. anthracis from the cutaneous lesions after administration of penicillin.

4. In vitro studies of the strain of B. anthracis isolated in 1 case showed it to be sensitive to the action of penicillin, but one hundred times less sensitive than a strain of Staphylococcus aureus.

5. A total of 100,000 units of penicillin is certainly the minimum effective dose, and a total of 200,000 to 400,000 units, given at a rate of 100,000 units per day, should serve to evoke a satisfactory therapeutic response in the average uncomplicated case of cutaneous anthrax.

6. Penicillin is a valuable agent in the treatment of human anthrax and deserves further clinical trial in this disease.

THE ROENTGEN DIAGNOSIS OF TRAUMATIC LESIONS OF THE CERVICAL SPINE

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Twenty-five hundred years B. C. a certain author stated that "one having a crushed vertebra in his neck, he is unconscious of his two arms and his two legs and he is speechless." Thus, according to Stinchfield,[1] began the history of fractures of the spine. As recently as 1917 an eminent radiologist said "On account of the technical difficulties in making plates laterally, most of us have been content to make stereoscopic plates in the anteroposterior projection." [2] Present day technic of cervical spine radiography is not difficult, if done with care.

In Percy Jones General Hospital we have been fortunate in having one of the newer developments in technical equipment—the Morgan meter.[3] This is valuable in making both simple and difficult projections of the spine. The operation of the meter depends on the fact that intensity × exposure time = a constant. Thus, if the intensity reaching the film is known in advance, the time for proper exposure can be determined algebraically. The Morgan meter does away with mathematical computations and the exposure time is read off directly from a calibrated scale on the meter. We have found the meter particularly valuable in taking various parts through casts and in other such cases where the examination for one reason or another may be considered technically difficult or where contrasty films are needed for any reason. With the aid of the Morgan meter excellent films of the cervical spine can be obtained through heavy plaster.

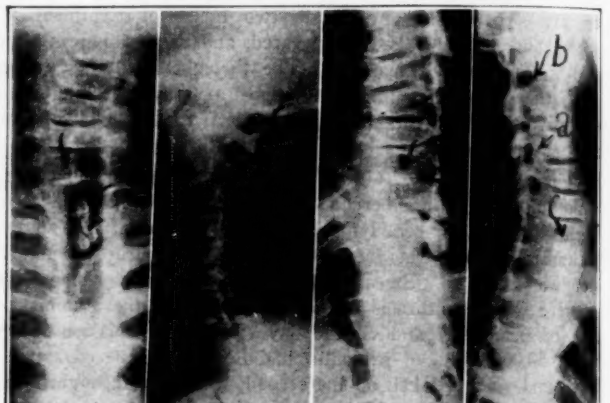

Fig. 1.—Conventional projections of cervical spine showing spina bifida occulta, calcified intervertebral disk and congenital fusion of second to third cervical and sixth to seventh cervical. Abnormal 8 shaped foramen at *a*; normal for comparison at *b*. Note the narrow intervertebral disk between sixth and seventh cervical. This is a frequent finding in patients without symptoms. (Courtesy of Capt. A. P. Dado.)

Read before the joint Section on Orthopedic Surgery and the Section on Radiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 16, 1944.

1. Stinchfield, F. E.: Fractures of the Vertebrae: A Five Year Collective Review, Surg., Gynec. & Obst. **70**: 378-388 (April) 1940.
2. Hickey, P. M.: Lateral Roentgenography of the Spine, Am. J. Roentgenol. **4**: 101-106 (March) 1917.
3. Morgan, R. H.: A Photoelectric Timing Mechanism for the Automatic Control of Roentgenographic Exposure, Am. J. Roentgenol. **48**: 220-228 (Aug.) 1942; Studies in Roentgenographic Exposure Meter Design, ibid. **48**: 88-98 (July) 1942.

In children one must bear in mind appearances mimicking fractures as a result of numerous ossification centers or areas of incomplete fusion.[4] In adults, running vertically in the region of the dens, one encounters radiolucent lines due to the superimposed interproximal space of the central incisor teeth. Separate ossicles

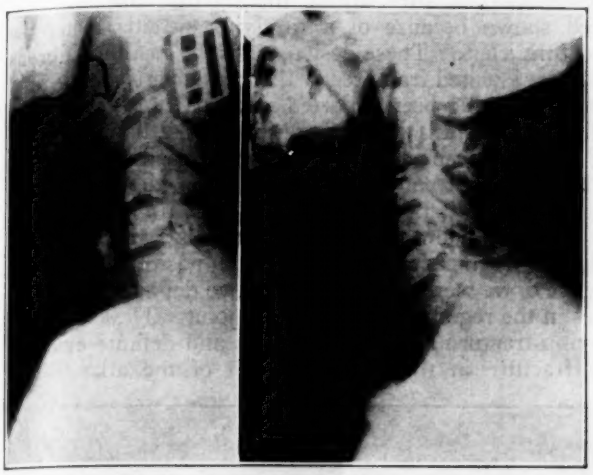

Fig. 2.—Gunshot fracture of second and third cervical vertebrae. A 0.25 caliber Jap bullet struck this patient in the mandible and the missile lodged in the neck. Twenty-four hours later he spat the bullet from his mouth. Note retrovisceral soft tissue swelling and bone spicules on the left. On right soft tissue swelling has returned to normal. Hypertrophic changes bridge the injured vertebral bodies. Very little ultimate disability resulted from this injury.

in the ligamentum nuchae may cause confusion, as will also the wedge shaped epiphysial deformity encountered with limbus vertebra. These are normal variants or at most the result of a disturbance of the ossification of the vertebral plates.

In addition to routine anteroposterior and lateral views made at 6 feet we often make films through the open mouth, oblique projections (50-55 degree rotation) and those in the Jackson position, which

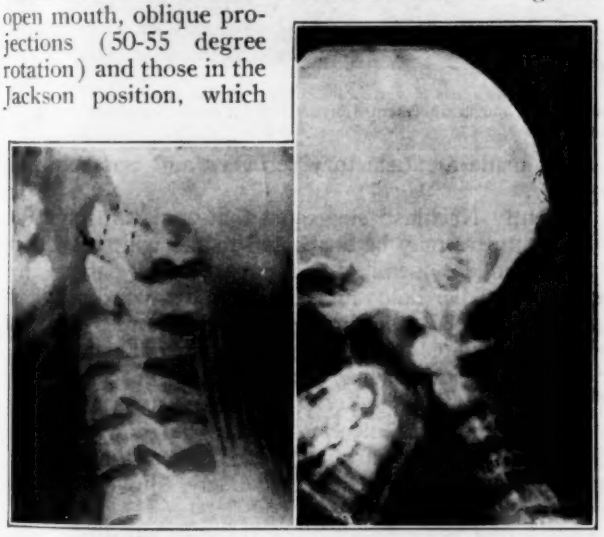

Fig. 3.—P. C. S., a private first class aged 21, was injured when thrown from a truck. Films showed fracture through the base of the odontoid with posterior displacement. Following head traction the deformity was completely corrected.

is similar to an exaggerated Waters view used in paranasal sinus examinations. It should be emphasized that the transoral view is essential in every case of neck injury. The less well known Jackson view is often helpful. The oblique views, as in figure 1, show the intervertebral foramens to best advantage. In certain instances fracture lines can be detected only in such projections. A normal intervertebral foramen has a smooth, oval appearance, while one with hypertrophic changes along its margins has an 8 shaped outline due to projecting osteophytes in its midportion. Hypertrophic changes may be of importance as a cause of symptoms and if located at or above the fourth cervical vertebral level may give rise to the swollen atrophic hand [5] without local cervical spine symptoms. Often numerous views are required before fractures in hypertrophic spurs can be demonstrated.[6]

Fractures of the cervical spine comprise 23 per cent of the cases of vertebral fractures examined in our department. They can be divided into two categories: 1. Those which affect the cord protecting portion of the spine; i.e., the neural arch and its processes. 2. Those which affect the weight bearing structures of the spine; i. e., the vertebral bodies. Vertebral body fractures may vary from minute spicules projecting

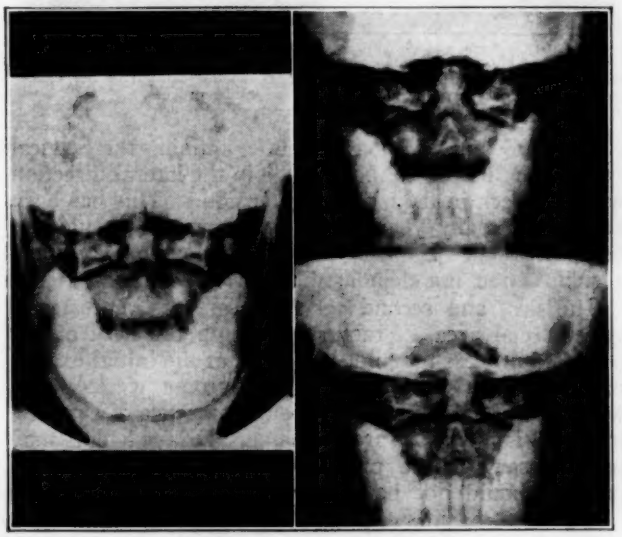

Fig. 4.—Transoral films showed the fracture line well visualized one month after the accident (see right hand illustration). This is due to presence of a rarefying osteitis.

anteriorly or a moderate bulge along the anterosuperior margin of the body to considerable compression of the spongy portion, with or without detached fragments. In the cervical spine—a relatively unprotected portion of the vertebral column—dislocations are often present and may or may not be associated with fracture. In sharp contradistinction is the dorsolumbar region, where dislocations are almost invariably associated with fracture. The soft tissues adjacent to the vertebral bodies must be carefully inspected. Any swelling of these structures indicates the presence of hemorrhage, edema or infection. In fractures of the arches, callus formation may be a prominent feature.[4]

The following case illustrates a compression fracture due to gunshot wound:

A private aged 23 was wounded by a sniper in New Guinea in December 1942. He crawled to a first aid station and twenty-four hours after the injury he spat a 0.25 caliber bullet out of his mouth. A comminuted compression fracture associated with pronounced swelling of the retropharyngeal structures

4. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis, Springfield, Ill., Charles C Thomas, Publisher, 1940, pp. 811 and 145-159.

5. Oppenheimer, A.: Swollen Atrophic Hand, Surg., Gynec. & Obst. **67**: 446-454 (Oct.) 1938.

6. Severance, R. D., in Discussion of Injuries to the Cervical Vertebrae, New York State J. Med. **42**: 615-619 (April 1) 1942.

resulting from hematoma was seen. A year later the fracture was well healed and bridged by osteophytes. On physical examination, minimal disability in flexion and extension was observed (fig. 2). Fortunately this patient escaped osteomyelitis, a not infrequent complication of gunshot wound in this area.

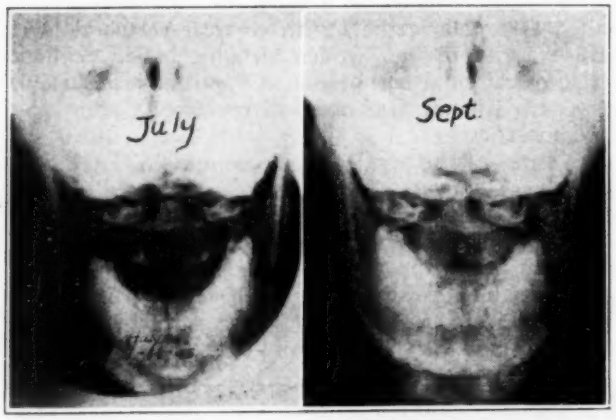

Fig. 5.—Abnormal distance between the lateral masses of the first cervical vertebra and the dens. This space should ordinarily not exceed one-half the transverse diameter of the odontoid process.

An important consideration in examining the cervical spine is the use of the films made in the lateral direction with the neck in flexion and extension.[7] This has been known for many years, but its importance should not be overlooked. Exposures made in flexion may show a subluxation not demonstrable in conventional views.

The first and second cervical segments represent a very special area. Fractures through the base of the odontoid process may not be shown at the initial examination and may be revealed only some weeks later, when additional studies indicate the presence of a rarefying osteitis along the fracture line. Delayed films may be necessary before proper diagnosis is made. The patient should not be accused of malingering on the basis of a single early negative examination. Fractures here may give rise to symptoms simulating those produced by the cord changes of primary pernicious anemia.

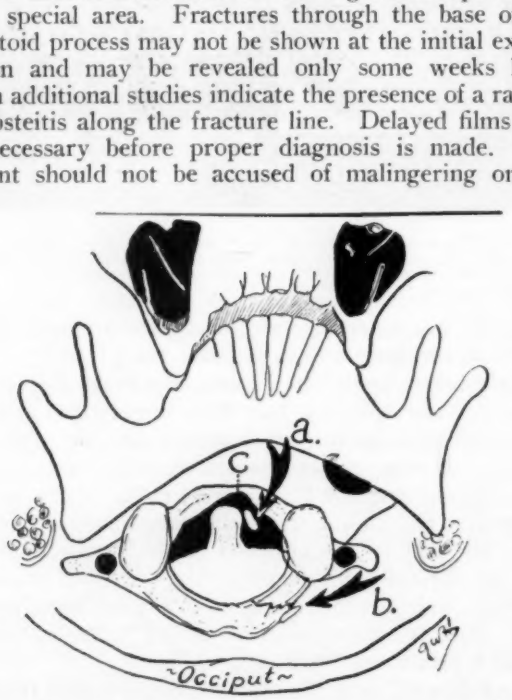

Fig. 6.—While walking in North Africa a private aged 24 was struck by a car. He was unconscious for six hours. A special film in the Jackson position showed a chip fracture of the odontoid at *a* and a fracture of the arch of the atlas at *b*. Same case as figure 5.

7. Pendergrass, E. P.: Personal communication to the author. Watson-Jones, R.: Fractures and Other Bone and Joint Injuries, Edinburgh, E. & S. Livingstone, 1940.

The roentgenologist must be conservative in interpreting films of this region, taking care to recognize definite abnormalities and by the same token avoiding false positive diagnoses. In the next case (figs. 3 and 4) there was a fracture of the dens with posterior luxation adequately corrected by head traction after six days. Seven months after injury the fracture line was still well shown because of a rarefying osteitis along the fracture cleft. These lesions usually heal by fibrous union. Isolated fractures of the atlas are relatively rare, only 99 having been reported since 1822.[8] The bilaterally symmetrical wide separation of the lateral masses of the atlas seen in figure 5 might be easily overlooked. The space normally present on each side of the dens does not ordinarily exceed one-half the transverse diameter of the odontoid process. In this particular individual, by means of the Jackson position shown in figure 6, we were able to identify two definite abnormalities in the region of the atloaxoid joint. These included a chip fracture lateral to the dens and definite evidence of fracture in the posterior arch of the atlas. This

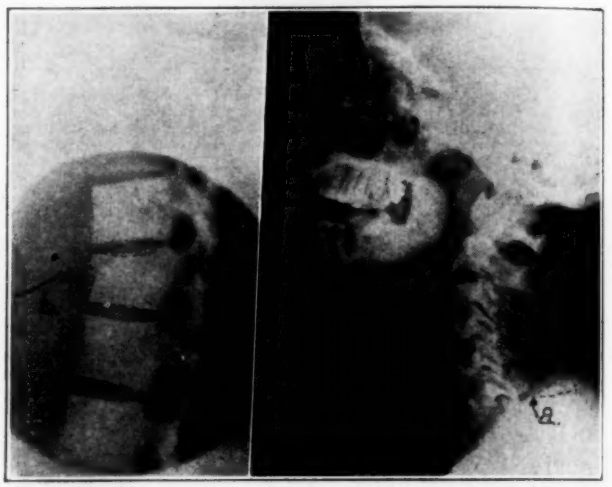

Fig. 7.—Two types of vertebral fracture: that of the posterior processes shown at *a* and crush fracture of the twelfth dorsal vertebral body at *b*.

patient made a satisfactory recovery and was returned to duty.

Recently Nachlas[9] suggested that arm pain of parachute jumpers may be attributed to the whiplash effect of the sudden opening of the parachute, particularly when the soldier holds his neck in an awkward position. In a review of 57 cases in the Royal Air Force, Hall and Morley[10] make the following significant statement: "Aircraft accidents may on occasion be appallingly destructive in their effects, yet it is surprising how much the human frame can tolerate and how often the pilots and co-pilots are uninjured when the machine may be totally wrecked. Conversely, slight accidents may have tragic results through sheer misfortune." Only 1 case of cervical spine fracture resulting from a flying accident is reported by them. Cervical spine fractures in parachutists are much less common than one might expect—approximately 2 in 10,000 jumps.[11]

The following case illustrates both categories of spinal fractures (injury of the posterior processes plus crush

8. Hatchette, S.: Isolated Fracture of the Atlas, Radiology **36**: 233-235 (Feb.) 1941.

9. Nachlas, W. I.: Brachialgia: A Manifestation of Various Lesions, J. Bone & Joint Surg. **26**: 177-184 (Jan.) 1944.

10. Hall, P. A., and Morley, G. H.: A Review of Cases of Injury to the Vertebrae Occurring in the Royal Air Force, Brit. M. J. **1**: 159-163 (Feb. 3) 1940.

11. Engelman, A. A.: Personal communication to the author.

fracture of the centrum), showing a break through the seventh cervical spinous process and a crush fracture at the dorsolumbar junction (fig. 7):

A staff sergeant was flying over New Georgia, when his plane was forced down by Japs. He parachuted to earth with his co-pilot, who had a broken arm due to gunshot wound.

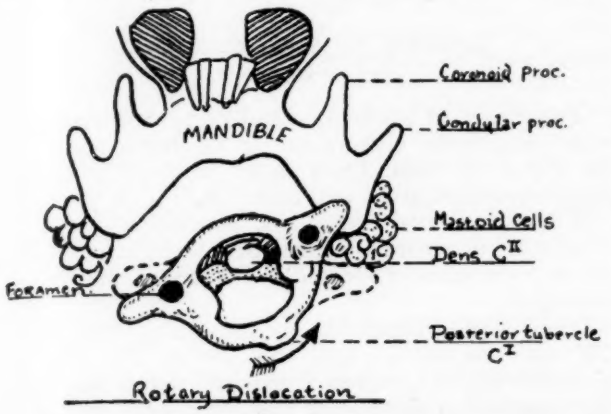

Fig. 8.—Roentgen anatomy of the Jackson position, showing the appearance of a proved case of rotary dislocation. Dotted lines indicate the approximate normal position of the transverse processes prior to dislocation.

They landed in enemy territory and heard Japs all around them but managed to crawl 500 yards through the jungle to the ocean and started swimming. The sergeant's abdomen became greatly distended because of ileus and both men were in a critical condition. They were rescued by friendly natives, who took them by canoe to a nearby island. Here they were able to communicate by radio with an army base and were picked up by a flying boat. Four weeks later the patient was receiving treatment in our hospital. This type of cervical spine fracture requires no surgical intervention. The dispatch with which this soldier was transferred to the zone of the interior needs no comment.

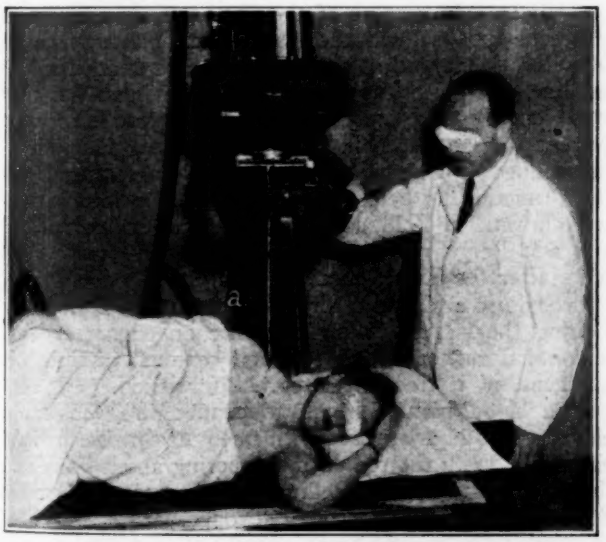

Fig. 9.—Position employed for cone down study of cervicodorsal junction. Pointer at *a*, showing position of central ray, is directed to the base of the cervical spine. For the left lateral projection, as indicated here, the left hand is placed on the head and the right shoulder is depressed. A satisfactory average technic with rotalix tube is 60-70-80 kilovolt peak, 100 milliamperes (one second at 100 milliamperes), medium sized telescopic cone. Bucky, focal distance 36 inches.

Another cervical spine lesion of importance is that of rotary dislocation of the atlas (fig. 8). This may be aggravated by trauma but often is the result of upper respiratory tract infection, especially when a cervical lymphadenitis is present. It is stated also to occur as a result of muscle spasm in poliomyelitis or when there is congenital absence of the dens or asymmetrical development of facets.[12] An illustrative case follows:

A private aged 23 who had two previous episodes of neck trauma had a tonsillectomy in February 1943. One week later he was returned to duty. In the latter part of March he complained of stiffness of the neck. Physical examination showed muscle spasm and enlarged cervical lymph nodes. A pronounced torticollis was present. Our x-rays showed a rotary dislocation of the axis on the atlas. Traction was employed, and in four days the muscle spasm subsided. Examination then showed the displacement corrected. While in traction he had radiculitis in the left arm and pain radiating to the front of the chest. A pantopaque myelogram failed to reveal evidence of a ruptured disk. In November the patient was up and comfortable, but considerable restriction of the motion of the neck was still present and roentgen examination showed some narrowing of the atlantoaxial joint.

Pathologic fractures of the cervical spine are of interest because of their rarity and must be differentiated from those caused by trauma:

A white man aged 56 complained of minimal pain at the base of his neck following a cystoscopy. The cervicothoracic junction was somewhat prominent. No point tenderness was noted.

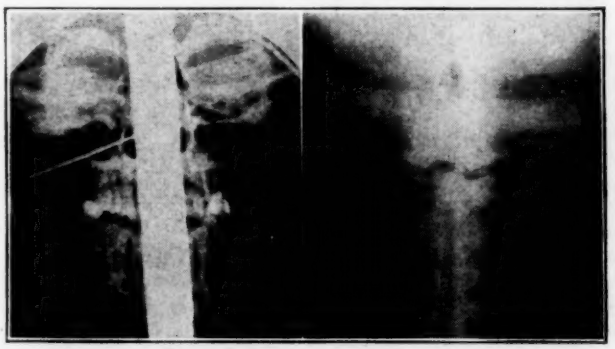

Fig. 10.—Film on left shows metal brace obscuring the odontoid. Film on right shows complete obliteration of brace as the result of laminagraphic study—section made at level of external auditory meatuses. There is an alteration in the normal contour of the dens due to fracture. (Courtesy High M. Wilson, M.D.)

Twenty-three days after cystoscopy a narrowed interspace was seen in the cervical spine films and the patient had an alternating low grade temperature with increasing pain in the distal cervical region. Special films were secured employing the technic shown in figure 9. These demonstrated a definite dislocation of the facets of the sixth and seventh cervical vertebrae. Films made after traction showed the segments in normal position with slight residual compression of the seventh cervical. These changes were felt to be the result of an osteomyelitis.

This case is included to stress the difficulties faced by the radiologist unless an adequate clinical history is available. The lower cervical segments are often difficult to visualize in short necked patients with heavy shoulders.

In certain instances the planigraph, or laminagraph, is of definite value. No dogmatic stand can be taken regarding such examinations, so much depends on the type of conventional films secured and their interpretation. The laminagraph is of importance in obliterating the shadow of metal braces or other orthopedic paraphernalia which in conventional films may obscure the anatomic detail.[12a]

In cases of pain referable to the cervical spine the diagnosis of a ruptured nucleus pulposus must be con-

12. Nicholson, J. T.: Spontaneous Reduction of Cervical Spine Dislocations, J. A. M. A. **115:** 2063-2069 (Dec. 14) 1940.
12a. Wilson, H. M.: Personal communication to author.

sidered. The intervertebral disk buffer may be disturbed by minimal traumas often repeated or by a single severe injury. Myelograms are done in our hospital in some such cases, Pantopaque (ethyl iodophenylundecylate) being the contrast medium used. The case illustrated in figure 11 presented a large filling defect at the level of the sixth cervical vertebra. This was proved at operation to be due to a herniated nucleus pulposus.

Experience with myelography indicates that successful delineation of such lesions is not always easy. Accurate diagnosis is dependent on several important factors:

1. Proper apparatus, including the use of a canvas support and a special attachment for obtaining lateral films in the prone decubitus.

2. Adequate extension of the neck to prevent the escape of the opaque material into the basal cisterns.[13]

3. Accurate spinal puncture by a neurosurgeon experienced in this type of procedure. This cannot be too strongly emphasized.

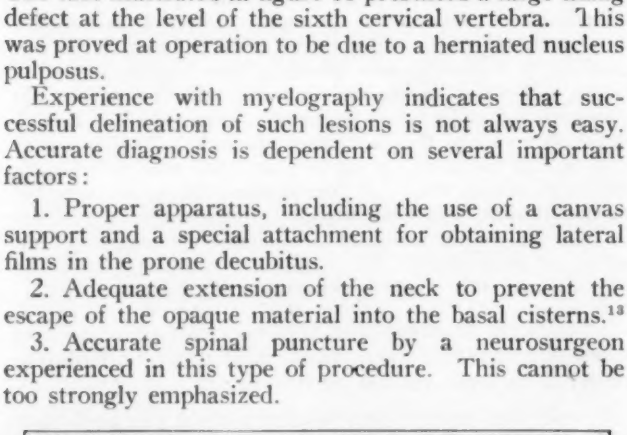

Fig. 11.—Defect produced by a large ruptured disk is shown on the right. Pain in shoulder and neck radiating down into first three fingers was made worse by coughing and straining. Minimal herniation is shown at left. Such a lesion could not be diagnosed without the aid of multiple films and close correlation of all the clinical findings. A small laterally placed disk was removed between the sixth and seventh cervical vertebrae with complete relief of symptoms. (Courtesy of R. Glen Spurling, lieutenant colonel, M. C., and Benjamin B. Whitcomb, captain, M. C.)

4. Proper withdrawal of the opaque medium at the completion of the examination to be checked by a scout film of the area examined.[14]

5. Lastly, and perhaps of most importance, the close correlation of clinical and radiographic findings.

CONCLUSIONS

1. The cervical spine, as the result of its relative lack of protection, is subject to many different types of injury.

2. The roentgen examination is an invaluable aid in diagnosis and differential diagnosis.

3. A thorough knowledge of the anatomy plus the roentgen technic indicated in the demonstration of various lesions is essential if the accurate diagnosis is to be attained.

13. Spurling, R. G., and Hampton, A. O.: Personal communication to the author.

14. Kubik, C. S., and Hampton, A. O.: Removal of Iodized Oil by Lumbar Puncture, New England J. Med. **224**: 455-457 (March 13) 1941.

POLYCYTHEMIA VERA

FINAL REPORT ON A CASE UNDER CONTINUAL TREATMENT WITH PHENYLHYDRAZINE HYDROCHLORIDE FOR ELEVEN YEARS

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AND
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SAN DIEGO, CALIF.

This is a final report on a case of polycythemia vera which was under observation for seventeen years, and for eleven of these years under continual treatment with phenylhydrazine hydrochloride. It is presented (1) because of the long period of treatment with the drug, (2) to record the changed blood picture during the last six years of life and (3) to report the autopsy findings.

Until a year before the patient died at the age of 72 years she led a useful and normal life. For the first eleven of the seventeen years the patient was under our observation the disease was successfully controlled, from the standpoint of the blood picture and subjective symptoms, by phenylhydrazine hydrochloride. Then, six years before death, a leukemoid type of blood picture developed. Three years before the change in the blood picture occurred a carcinoma of the cervix had developed which was effectively treated with radium. The radium had only temporary, if any, effect on the blood picture. The physical findings remained much the same as at the time of our last report in 1932.[1] In appearance the patient had aged. Her color, even up to the time of her death, would have led a trained observer to suspect the presence of polycythemia vera. The heart apparently became somewhat enlarged and there was evidence of mild myocardial and vascular degeneration; the blood pressure remained within normal limits. There was slight enlargement of the liver but no more than would be expected with the heart and circulatory changes or with an enlarged spleen. The spleen extended to the midline and almost to the crest of the ilium but this represented no appreciable change in size since the patient was first seen in 1924. The kidney function as determined by the phenolsulfonphthalein test and the liver function as determined by the hippuric acid test were normal in 1938, as were the icterus index and the van den Bergh reaction. Analysis of the gastric contents after the Ewald meal revealed an absence of free hydrochloric acid and a total acid content of 9 degrees. During the last few months of life an edema and an abdominal ascites which required removal of fluid by paracentesis at frequent intervals developed.

The blood picture began to change in 1935, after eleven years of treatment with phenylhydrazine hydrochloride. With the red cells numbering about 7 million the patient started her medication as usual. This time the number of red blood cells dropped from 7 million to 4 million, a slightly greater response to the drug than had been normal for her. Then, instead of the usual gradual increase in red cells with the withdrawal of the drug, there was a continued decrease to between 2 and 3 million, at which level they remained for the remaining six years of the patient's life. The hemoglobin concentration of the blood, which had varied from 12 to 17 Gm. per hundred cubic centimeters, fell in like

From the Rees-Stealy Clinic.

1. Stealy, C. L.: Polycythemia Vera: Report of Case Treated with Phenylhydrazine Hydrochloride over Period of Seven and One-Half Years, J. A. M. A. **98**: 1714-1716 (May 14) 1932.

manner to a level of 7 to 9 Gm. per hundred cubic centimeters. The presence of normoblasts was noted and poikilocytosis, polychromatophilia and achromia appeared. The leukocyte count, which had previously maintained a high level of 15,000 to 20,000 with occasional jumps to 25,000 and 30,000, dropped with the red cell count and during the last five years ranged between 5,000 and 10,000 with an occasional rise to 12,000 or 13,000. The first myelocytes appeared in the blood smear at sporadic intervals two years before the red cell count dropped and became a constant finding during the last six months of phenylhydrazine therapy. The possibility of the development of a primary anemia was considered in view of the lack of gastric acid even though the blood picture was not typical, but there was no reticulocyte response to liver therapy. It has been observed by others that the gastric acid falls with increasing polycythemia [2] but that the antianemic principle of Castle which is absent in pernicious anemia is present in excessive amounts in polycythemia vera.[3]

The blood picture suggested the development of a leukemia, but microscopic examination of the blood smear did not bear out such a diagnosis. Dr. Charles A. Doan of the Department of Medicine at the Ohio State University College of Medicine, who examined some of the blood films wrote:

I was particularly impressed by the changes in the red blood cells. There was marked variation in size and shape of the erythrocytes, and a definite polychromatophilia and achromia. There was an unusual number of red cells showing punctate basophilia, sometimes 2 or 3 being seen in a single oil immersion field. There were many microcytes and occasional macrocytes. The average diameter as revealed by the Eve halometer was 7.64 microns. The blood platelets were, for the most part, sparsely scattered as single units and varied strikingly in individual size, there being microthrombocytes as well as macrothrombocytes. As far as the white cells are concerned, I should feel that the findings were indicative of a definite myeloid hyperplasia of the marrow, primarily of the neutrophilic granulocytes. The percentage of myeloid elements together with the very definite "left shift" principally to the band form stage, with only 6 per cent actual myelocytes present, and no increase in basophils or eosinophils, does not bespeak an active leukemic process. Furthermore, the quality of the myelocytes is not suggestive of a leukemic anaplasia. The lymphocytes show a moderate degree of "left shift" not pathognomonic. . . . The presence of an occasional nucleated red cell, the very marked polychromatophilia, and especially the degree of punctate basophilia, when coupled with marked size and shape changes, and 12 per cent of toxic granule neutrophils among the white cells, could only be interpreted as a reflection of a toxic hemolytic destructive agent.

A year later blood films were again sent to Dr. Doan. He saw no change in the general hematologic picture and interpreted the findings as "representing very active myeloid and erythroid activity in the bone marrow under some disadvantages, toxic or otherwise, together with an accompanying disturbance in the normal function of the megakaryocytes; that is to say, an abnormality which affects all of the active hemopoietic elements in the bone marrow."

There was little change in the blood picture from this time until the death of the patient in 1941. The following is a representative blood count of this period: hemoglobin concentration of the blood 9 Gm. per hundred cubic centimeters, erythrocytes 2,900,000 and leukocytes 7,800. The leukocytes were differentiated as follows: neutrophils 80 per cent, of which 53 per cent were band forms, 25 per cent segmented forms and 6 per cent myelocytes; lymphocytes 14 per cent; eosinophils 1 per cent, and basophils 1 per cent. There was 1 normoblast to every 100 erythrocytes.

The necropsy report is given in its entirety:

The arterially embalmed body was that of a quite emaciated white woman, 67 inches (170 cm.) long and weighing about 90 pounds (41 Kg.). The abdomen was distended and showed an old low midline scar. There was moderate edema of the feet and legs. The superficial lymph nodes were not enlarged. The tissues gave the appearance of anemia.

The brain showed moderate atrophy of the convolutions with widening of the sulci but otherwise was normal. The meninges appeared normal. The arteries were moderately sclerotic. The pituitary gland appeared normal.

There was a small amount of clear fluid in both pleural cavities. The lungs showed only hypostatic congestion. The heart was normal in size. The epicardium showed an area of edema at the apex but otherwise the heart was normal. The aorta was moderately sclerotic. The mediastinal lymph nodes were not enlarged.

The abdominal distention was due to a large quantity of clear yellow fluid. The mesenteric, gastric, splenic and esophageal veins were greatly enlarged. A segment of small intestine was adherent to the old scar. The peritoneum was smooth but somewhat opaque. The spleen extended to the brim of the pelvis (1,950 Gm., 25 by 5 by 10 cm.). The surface was rough and dull gray with several yellow patches (2 to 5 cm.) which were the sites of infarcts. The consistency was firm and fibrous. The cut surface was dull brown with white fibrous bands. The capsule was 2 mm. thick. The liver was somewhat enlarged (1,820 Gm.) and firm, and the edge was rounded. The surface of the right lobe was fairly smooth. A great part of the left lobe showed a nodular surface. It cut with increased resistance, the cut surface being pale in appearance and homogeneous. The capsule was thickened. The gastrointestinal tract and pancreas appeared normal. The surfaces of the kidneys were granular, the capsules adherent. On the cut surfaces the markings were distinct, but the cortex was reduced in thickness. The adrenals appeared normal. The bladder and ureters were normal. The uterus, tubes and ovaries had been surgically removed in the distant past. The mucosa over the vault of the vagina was smooth. There was a fibrous nodule which was regarded as the remnant of the cervix uteri, the os having been destroyed by radium treatment.

There were no enlarged pelvic lymph nodes. The aortic chain of nodes and the hilar nodes of the spleen were quite large (2.5 by 1.5 by 1 cm.), firm and of fibrous consistency. Those about the spleen were brownish red (pigment). The marrow in the middle third of the tibia and femur was deep red and quite firm. The vertebral marrow was similar in appearance.

On microscopic examination, the spleen showed marked fibrosis. The follicles were widely separated. Myeloid cells, including an occasional megakaryocyte, were present but not in large numbers. There was a considerable quantity of phagocytized pigment. The lymph nodes were quite fibrotic, with thickened capsules. The lymphoid tissue appeared as islands separated by fibrous bands. The germinal centers were small and inconspicuous. There were myeloid cells including an occasional megakaryocyte scattered through the sections. There was considerable phagocytized pigment. This was quite extensive in the splenic nodes. The reticulum was not increased.

The bone marrow presented the picture of myelosclerosis with fibrosis and vascularization. It was relatively deficient in hemopoiesis except for megakaryocytes of all sizes, which were present in great excess. Phagocytic cells with ingested pigment were fairly numerous. The marrow was engorged with erythrocytes.

Periportal fibrosis in the liver varied in intensity in different areas. It was most marked in the left lobe. There was atrophy of the liver cells and many areas of fatty degeneration. Small

2. Apperly, F. L., and Cary, M. Katherine: The Relation of Gastric Acidity to the Erythrocyte Content of the Blood, Am. J. Digest. Dis. **3**: 466, 1935.
3. Adamson, W. B., and Storey, J. E.: Observations on Etiology of Polycythemia Vera, Texas State J. Med. **36**: 26-29, 1940.

infiltrations of myeloid cells and lymphocytes were most prominent beneath the thickened capsule.

Numerous sections through the stump of the cervix showed nothing to indicate a previous malignancy. The kidneys, pancreas, adrenals, heart, lungs, brain and hypophysis showed nothing noteworthy. The infiltrations of myeloid cells in the spleen, liver and lymph nodes were regarded as being not extensive enough to suggest a leukemic process. No sections showed anything suggestive of metastatic carcinoma.

Summary: cirrhosis of the liver with ascites; splenomegaly with fibrosis and infarction; myelosclerosis; lymphadenopathy; myeloid infiltrations in liver, spleen and lymph nodes; healed carcinoma of cervix uteri.

COMMENT

After eight years of treatment with phenylhydrazine hydrochloride in this case, we concluded[1] (1) that, once the necessary dosage was established for an individual patient, the patient would respond to that dosage consistently, (2) that the patient does not acquire a tolerance to the drug and (3) that the drug apparently produces no deleterious effect on the liver and kidneys. Observation of the patient for the remaining nine years of her life, during the first three of which treatment with phenylhydrazine hydrochloride was continued, did not change the first two of these conclusions. The final outcome of the case and the necropsy findings make it impossible to say conclusively that the drug had no deleterious effect on the liver. However, neither can we hold the drug responsible for the cirrhosis which finally developed, for serious liver damage is known to occur in cases of polycythemia in which the drug has not been used. We can only state that after eleven years of treatment with phenylhydrazine hydrochloride no evidence of liver damage, aside from palpable enlargement of the liver, which is a frequent accompaniment of an enlarged spleen, could be demonstrated. Changes in the hemopoietic system such as those which took place in this case have been reported also in cases not treated with phenylhydrazine, so that these cannot be considered effects of the drug. From our observation of this case, in the light of our present knowledge of the disease and its control, we feel that, in the absence of the usual contraindications to the use of the drug, phenylhydrazine hydrochloride offers a satisfactory form of treatment for polycythemia vera.

The possible relationship between polycythemia and leukemic processes, their concurrent presence in the same patient and the apparent shift from one to the other in some cases have been discussed in many excellent articles. The necropsy findings in our case, both on macroscopic and on microscopic examination, were no more diagnostic of a myelogenous leukemia than were the changes in the blood picture. We can describe them only as leukemoid rather than leukemic in character. Dr. Doan, whose interpretation of the blood films in the case we have already quoted, and Dr. Roy R. Kracke of Emory University reviewed these sections. Both concurred with our conclusions. Dr. Doan wrote "I certainly can find no evidence in any organs studied or in sections available of anything that would lead me to make a diagnosis of myelogenous leukemia." In commenting on the bone marrow he said "I had rather the impression of exhausted or 'burned out' or toxically inhibited myelopoietic activity in the marrow." Dr. Kracke's impression was "that this was a case of polycythemia vera of years' standing which terminated with a leukemoid reaction and anemia."

Based on a review of 163 cases of polycythemia vera, Tinney, Hall and Giffin[4] felt that the degree of splenomegaly and the presence of a leukemoid reaction were directly correlated with the duration of the polycythemia, although they did not consider their data in this series sufficient to prove this. We are inclined to believe that the change in the blood picture of our patient represents the usual outcome of all cases of polycythemia vera of sufficient duration. The true nature of the underlying process remains to be determined.

PRACTICAL CONSIDERATIONS

A case of polycythemia vera was under observation for seventeen years. For the first eleven years of this period, until a definite change in the blood picture occurred, the disease was apparently controlled by phenylhydrazine hydrochloride. The extensive liver damage which was found at autopsy six years later was not evidenced until the last year of life. Since both hemopoietic changes and liver damage have been reported in cases not treated with phenylhydrazine hydrochloride, the possibility of the development of these conditions would not appear to be a contraindication to the use of the drug. The changes in the blood picture, which may constitute a part of the disease process in cases of sufficient duration, are not clearly understood at the present time.

Clinical Notes, Suggestions and New Instruments

ACUTE EPIDURAL ABSCESS OF THE SPINAL CANAL

COMPLETE RECOVERY FOLLOWING EMERGENCY LAMINECTOMY AND PENICILLIN

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Death from acute epidural abscess of the spinal canal is needless. It is important, however, that an early diagnosis of the abscess be made and decompressive laminectomy effected. This obviates the pressure which produces in the lumbar region, if unrelieved, rapid paralysis of the legs and urinary bladder. If many hours are lost after paralysis and anesthesia of the legs have become complete, permanent paraplegia, if not death, results.

An observing doctor will seldom miss an epidural spinal abscess. The patient, recovering from multiple boils, begins to have an unexplained fever. There next develops a severe pain in the back. If a blood count is made, a pronounced leukocytosis is present. The fever continues and soon there is tenderness over the spine. Urinary retention ensues and there develops a complete paraplegia with loss of all sensation below the level of the lesion. All these signs and symptoms have occurred within forty-eight hours of the onset of pain in the back.

Surgical intervention must now be employed, else the patient dies from an extending infection, i. e. pyemia or ascending pyelonephritis. At this stage, spinal puncture can verify the presence of an abscess of the spinal canal. A very cautious tap, however, is necessary with repeated removal of the obturator and aspirating as the needle advances. If pus is encountered, the needle is withdrawn and steps for an immediate laminectomy are taken. If the site where the puncture is made is free of pus, the needle can be advanced into the subarachnoid space. The demonstration of a spinal fluid block is indicative of an

4. Tinney, W. S.; Hall, B. E., and Giffin, H. Z.: The Liver and Spleen in Polycythemia Vera, Proc. Staff Meet., Mayo Clin. **18**: 46-48, 1943.

From the Division of Neurosurgery, University of Tennessee School of Medicine, and the Fort Sanders Hospital Surgical Service at Fort Sanders Hospital.

extradural abscess and not an infection of the cord, per se. The pus and granulation tissue removed, plus the decompressive measures afforded by laminectomy, relieve the pressure on the cord and help the circulation to reestablish itself.

The incidence of the epidural spinal abscess is unknown. In 1926 Dandy [1] stated that he had had no patients with an epidural abscess nor had he seen the condition at necropsy. He found, after reviewing the literature, 25 cases which had occurred and been reported. Many more cases have been reported since Dandy made his survey and made his worth while contribution to knowledge of the anatomy of the epidural space.

ANATOMY

The epidural space is dorsal to the spinal roots; there exists no space ventrally, as the dura is firmly adherent to the vertebrae in this location. Only a potential space exists in the cervical region. From the seventh thoracic to the second sacral vertebrae, where the space ends, the size is variable, being widest in the midthoracic and midlumbar region. These anatomic facts are cited to explain the frequency with which inflammatory processes localize in either the midthoracic or the midlumbar region. Fat, areola tissue and blood vessels fill the epidural space.

ETIOLOGY

The majority of abscesses arise by metastasis from furuncles of the skin via the blood stream. It is possible, however, for them to occur by direct extension from suppurating lesions in the adjacent tissue. While boils are the most common etiologic factor, as reported by Gasul and Jaffé,[2] the source of the organism was unknown in 17.9 per cent of these cases, but there was history of trauma.

The staphylococcus is the organism that is responsible in the majority of cases; however, Delearde [3] reported a case caused by the streptococcus and Schick [4] reports 1 caused by the pneumococcus.

DIAGNOSIS

An epidural abscess of the spinal canal should be suspected when a patient with furuncles or a history of trauma begins to show an elevated temperature and have root pains in the back and weakness of the legs. Weakness of the legs alone forces us to rule out tumors of the canal with compression of the cord. Pott's disease must also be considered. All these conditions are afebrile. If, on the other hand, elevated temperature exists and epidural abscess is ruled out, then one considers infectious myelitis and poliomyelitis. To rule out the latter two conditions in which no block exists, a Queckenstedt test is done using the simple manometer which measures pressure in millimeters of water.

To determine the level at which to operate, one depends on tenderness of the spine on palpation and establishment of a definite sensory level by careful neurologic examination. In epidural abscesses of the cord, a lumbar tap is not without danger. The cautions just mentioned should be rigidly adhered to else there is the possibility of the point of the needle being carried into the subarachnoid space with resultant meningitis.

TREATMENT

No time is left for procrastination, once diagnosis of an epidural abscess with compression of the cord is made. Since destruction of the spinal cord is out of proportion to the amount of compression, the laminectomy is extended in both directions until the lesion is exposed in its entirety. When the upper limit of the pathologic area has been reached and the area is cleared of pus and granulation tissue, the cord will begin to pulsate. The dura is not opened. After removal of as much of the granulation tissue and pus as possible has been accomplished, adequate drainage of the epidural space is assured by placing a small penrose drain on the surface of the dura. The wound is frosted with sulfathiazole powder and closed loosely, thus encouraging granulation from the bottom. I feel that when the causative organism is the staphylococcus, the streptococcus or the pneumococcus, as determined by direct smear, penicillin is of prime importance and should be started immediately.

PROGNOSIS

Cases in which recovery occurs without the benefit of surgery are the exception and very rare. When surgical intervention has been carried out before the paralysis has been complete for more than a few hours, there is a chance for some recovery. In 60 cases of Abrahamson,[5] survival occurred in 20 of the 30 cases in which operation was performed. Of the 30 patients not operated on, none survived. If operation is delayed until paralysis has been complete for a number of days, Echols [6] states that operation is usually contraindicated.

Patients operated on after paralysis has been complete for as long as twelve hours usually recover enough to walk and control the sphincters, yet usually retain residual motor disturbances.

REPORT OF CASE

M. W., a white girl aged 12 years, was admitted to Fort Sanders Hospital in Knoxville, Tenn., June 6, 1944 complaining of pain in the lower part of the back radiating into the chest. About three weeks before, the patient had a severe blow to her buttocks, the result of a fall from a teeter board. One week before entering the hospital she was confined to bed because of pain in the buttocks. A few days later the pain was in the lower part of the back and was very severe. The night before admission to the hospital the patient was still ambulatory, but there was a noticeable foot drop and walking was difficult. It was necessary to catheterize her to obtain a specimen of urine, as she was unable to void spontaneously. Eight hours after admission to the hospital the child had developed a complete paraplegia and a paralyzed bladder. A neurologic consultation was then requested.

Examination divulged an oral temperature of 103 F., nuchal stiffness, abdominal distention and tenderness, flaccid paralysis of the lower extremities and anesthesia downward from the level of the inguinal ligament bilaterally, with pronounced tenderness over the twelfth thoracic and first and second lumbar spinous processes. A cautious lumbar puncture was done with negative pressure being maintained by using a 2 cc. Luer syringe attached to the spinal needle. When thick pus was aspirated extradurally, the needle was immediately withdrawn.

Three hours later, under general anesthesia, the spines and laminas of the eleventh and twelfth thoracic and first, second and third lumbar vertebrae were removed. As soon as the ligamentum flavum was incised, pus welled up into the wound. The area exposed was cleaned of granulation tissue and pus. at the end of this procedure the cord was pulsating nicely. A rubber tissue drain was placed in the wound and on the dura, the operative site sprinkled with sulfathiazole and closed loosely. Four hundred thousand units of penicillin was given intramuscularly, 12,500 units every three hours until the temperature was normal for a period of twenty-four hours.

On the eleventh postoperative day, the patient was able to move the toes of both feet and could discern a pinprick to just below the knee bilaterally. On removal of the indwelling catheter the patient was able to void after being given an ampule of a preparation of carbaminoylcholine chloride. Three days later urination was normal. Twenty days postoperatively sensation was normal in both legs and there remained only slight muscular weakness of the lower limbs. By the twenty-fifth postoperative day the wound had healed by secondary intention and the child was dismissed from the hospital. The patient was seen on the thirty-first postoperative day and no muscular weakness remained. Sensation was normal in both legs in their entirety.

1004 Medical Arts Building.

1. Dandy, W. E.: Abscesses and Inflammatory Tumors in the Spinal Epidural Space (So-Called Pachymeningitis Externa), Arch. Surg. **13:** 477 (Oct.) 1926.
2. Gasul, B. M., and Jaffé, R. H.: Acute Epidural Spinal Abscess: A Clinical Entity, Arch. Pediat. **52:** 361, 1935.
3. Delearde, A.: De la périméningite aigue spinale, Gaz. hebd. de méd. **42:** 493, 1900.
4. Schick, K.: Pachymeningitis spinalis externa purulenta als Metastase nach Diplokokkenbronchitis, Wien. klin. Wchnschr. **22:** 1185, 1909.
5. Abrahamson, L.; McConnell, A. A., and Wilson, G. R.: Acute Epidural Abscess, Brit. M. J. **1:** 1114, 1934.
6. Echols, D. H.: Emergency Laminectomy for Acute Epidural Abscess of the Spinal Canal, Surgery **10:** 287, 1941.

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT OF THE COUNCIL

The Council has authorized publication of the following report. The outline in this report is offered as an objective, a pattern and not a regulation. However, it has been adopted for publication with the belief that it will be of help to manufacturers and scientists who undertake the investigation of new drugs.

Austin Smith, M.D., Secretary

LABORATORY AND CLINICAL APPRAISAL OF NEW DRUGS

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A new drug should pass through several phases of investigation before it is declared suitable for distribution in commerce. It should be studied in the laboratory and in the clinic, the details of the study depending on the nature of the ingredients and the intended uses, but all investigations should follow a general plan which will permit a thorough understanding of the usefulness and toxic properties of the drug.

In considering new drug applications in the enforcement of the Federal Food, Drug and Cosmetic Act, the Food and Drug Administration is concerned primarily with evidence of safety. The Council on Pharmacy and Chemistry is concerned not only with the evidence of safety but also the evidence adduced to support the claims made for new drugs. Too frequently this evidence is found inadequate and the sponsors of new preparations, if they wish to provide the missing data, may find it necessary to repeat some of the more time consuming and expensive procedures and at other times find it advantageous to proceed along entirely new lines of thought. If the manufacturer has adequate facilities for laboratory and clinical appraisal, he can usually obtain the desired information within a reasonable period. Frequently however such facilities are not immediately available and much effort must be spent in searching for appropriate channels for investigation. If a comprehensive outline had first been prepared and then closely followed, loss of time and expenditure of needless effort might have been avoided.

At the same time it is an advantage for physicians and allied scientists to know by what standards a new drug has been evaluated. When the physician is urged to use this agent, he should have available such evidence as will satisfy his questions concerning safety and efficacy.

The activities of the Council on Pharmacy and Chemistry of the American Medical Association in this field have recently been described.[1] Certain phases of the activities of the Food and Drug Administration which bear on this problem have also been published or are in press.[2]

The Council on Pharmacy and Chemistry has provided for almost forty years a set of rules to guide manufacturers for the submission of articles for inclusion in New and Nonofficial Remedies. At periodic intervals it has enlarged on these rules to provide criteria such as those found acceptable for the evaluation of skin disinfectants and contraceptives.[3] Usually the criteria have been concerned with one special agent or class of agents. The Federal Food, Drug and Cosmetic Act provides that applications for new drugs shall contain "full reports of investigations which have been made to show whether or not such drug is safe for use," and the Food and Drug Administration provides a form in which are set forth suggestions concerning the scope and character of these reports.

If the utmost of possible benefits with a minimum of possible dangers is to result when a new drug is introduced for experimental trial and later in commerce, it is necessary to develop methods of appraising the therapeutic usefulness and potential harmfulness of new drugs and to organize these methods into a logical system which, if followed, will give reasonable assurance that the new preparation will not be offered to the medical profession or to the public before the extent of its usefulness or the potentialities for harm are understood. The present paper outlines the principles which have been helpful in making such an appraisal of new drugs.

PRELIMINARY OBSERVATIONS

The preliminary experimental observations with a new agent give the clue to the possible field of usefulness. In dealing with chemotherapeutic agents, these preliminary observations consist usually of tests of the efficacy of the agent in combating or preventing some experimental infections. In the case of drugs that might be termed "symptomatic agents," the preliminary observations should include tests of the possible pharmacodynamic actions of the drug. These observations "set the sights," so to speak, and indicate the course to be pursued in subsequent and more detailed investigations.

LABORATORY OBSERVATIONS

Assuming that a new drug has shown promise in the preliminary tests, more extensive inquiry must now be made into the mechanisms of its action and its

The authors wish to express their appreciation of the helpful comments offered by Dr. Torald Sollmann, Dr. P. J. Hanzlik and Dr. A. L. Tatum.

1. Smith, Austin: Membership, Activities, Method of Operation, Attainments of the Council, J. A. M. A. **124:** 433 (Feb. 12) 1944.
2. Woodard, Geoffrey, and Calvery, Herbert O.: Acute and Chronic Toxicity, Industrial Med., January 1943. Calvery.[4] Van Winkle.[6] Draize, Woodard and Calvery.[5]
3. Contraceptive Agents, Report of Council on Pharmacy and Chemistry, J. A. M. A. **123:** 1043 (Dec. 18) 1943; Criteria for Evaluation of Skin Disinfectants, ibid. **121:** 593 (Feb. 20) 1943.

toxicity. In order for the clinician to use a drug intelligently he must know the manner in which its effects are brought about. The plan of procedure and the details of the tests to be employed should be formulated in accordance with the type of agent to be investigated, e. g. single chemical entity, complex extract, hormone, serum or vaccine. The conditions in which the drug is thought to be useful and the observations made in the preliminary testing will also modify the plan of investigation and the details of the test procedures. Nevertheless we feel that the following general types of study should prove to be applicable to most new drugs, keeping in mind that these are suggestive and not necessarily exhaustive:

(A) *Biochemistry.*—General properties of drug, including solubility, stability; studies of absorption, reabsorption, fate, distribution and excretion of the drug; quantitative data on these points where possible; mode of detoxification (excreted unchanged, oxidized, reduced, acetylated?); effect on enzymes, blood and tissues; chemistry of body fluids and tissues; production of toxic products during course of metabolism.

(B) *Pharmacodynamics.*—Local: Tests of irritation on skin, eye, alimentary canal; intradermal irritation, sensitivity or anesthesia; tests of protoplasmic depression or toxicity, and reversibility of effects on cilia, nerve trunks, mucosa; hemolysis, antihemolysis and blood pigment changes.

Systemic: Action on blood pressure, respiration, muscles, nervous system, cardiac functions, secretions, temperature, voluntary activity, organ perfusion, isolated tissues; effects of vasomotor agents, proteins, fats, metals, solvents and other agents on the actions of the drug; cumulative effects; development of tachyphylaxis; quantitative and qualitative differences in action in different species of animals.

(C) *Experimental Functional Pathology.*—Effects in experimentally induced pathologic states, e. g. smooth muscle spasm, hypodynamic hearts, fibrillations and arrhythmias, hypertension, respiratory depression, edema, shock, burns, anemias.

(D) *Chemotherapeutic.*—Effects in preventing specific experimental infections; effects in combating experimental infections or actions of toxins; antagonists of chemotherapeutic agents, e. g. pus, serum, tissue products; distribution in inflammatory states, e. g. meningitis, dermatitis; minimal effective dosage (ED50).

The data obtained from these studies will serve as a guide in the clinical application of the product and doubtless will also show evidence of undesirable or potentially harmful effects. If such effects are not observed, a careful search must be made for them. This involves the very important study of the toxicology of the preparation. Woodard and Calvery,[2] Calvery [4] and Draize, Woodard and Calvery [5] have set forth in considerable detail the approach to the study of the acute and chronic toxicity of drugs and other chemical agents. Certain of the principles which they have formulated bear repetition here, and the original publications can be consulted for more detailed discussions.

Depending on the conditions for which the product may be used, on its biochemical and pharmacodynamic actions and on the methods of its use, adequate studies of its toxicity must be made. The following outline sets forth in general terms the scope that these studies should embrace:

(A) *Acute Toxicity.*—Dosage response curves in three or more species; objective symptoms; statistical calculations for comparative studies; simultaneous comparative determinations of other substances; variations in toxicity with method of administration.

(B) *Subacute Toxicity.*—Large daily doses to one or more species for six to twelve weeks; microscopic pathology.

(C) *Chronic Toxicity.*—Three or more species; at least one species for the life of the animal; several dosage levels graduated to produce from no effect up to pronounced lesions, and possibly shortening life span; microscopic pathology; effects on voluntary activity, e. g. running or other performance as evidence of more subtle functional changes.

(D) *Local Effects.*—Sensitization; skin irritation; mucous membrane irritation; photosensitization.

(E) *Special Studies.*—Reproduction; distribution and storage; effect of diet; effect of environment; kidney and liver function tests.

In selecting animals for investigation of new drugs it is important to use several distinct species, since it is well known that qualitative as well as quantitative differences exist between animal species in their reactions to drugs. Some species are wholly unsuited for demonstration of certain effects; e. g. methemoglobin is not readily produced in rodents and if the drug is suspected of causing this reaction rats, rabbits and guinea pigs are not suitable test animals. Rabbits are not usually satisfactory animals for blood pressure studies and often react atypically; e. g. histamine produces a rise of pressure instead of a fall. Emetics cannot be tested in rodents, since vomiting does not occur in these species. Many other examples could be cited, but these suffice to demonstrate the need for careful selection of suitable test animals.

Each investigator, including those concerned with clinical as well as laboratory investigations, should realize from the beginning where each specialty fits in the over-all plan of study; e. g. chemistry, pharmacology, physiology, pathology. He should keep a careful record of all data and not be guided solely by impressions. The records should include actions not seemingly connected with the immediate project and dramatic response; for example, micturition, defecation, vomiting, pulse, respiration.

After completion of the experimental studies, a critical review of the accumulated data should be made. The purpose in this review is to reach a decision as to whether clinical trial of the drug is justified. It is difficult to set forth criteria on which this decision should be made, since the judgment of the investigators must always be an important factor. However, without any claim for completeness, the following points should be considered:

1. Has the drug definite and desirable pharmacodynamic or chemotherapeutic actions?

2. Are its actions constant and reproducible?

3. Are these actions observed in different species of animals?

4. Is the mechanism by which its actions are produced a desirable one, or are the actions the result of an ultimately undesirable reaction of the animal?

5. Are the effects obtained in animals in which experimentally produced pathologic or functional changes comparable to human diseases have been made?

6. What is the therapeutic index of the compound (ratio of effective dose to toxic dose: ED50/LD50)?

4. Calvery, Herbert O.: Safeguarding Foods and Drugs in Wartime, Am. Scientist **32**: 103-119, 1944.

5. Draize, John H.; Woodard, Geoffrey, and Calvery, Herbert O.: Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes, to be published.

7. Are the undesirable side actions of sufficient importance and severity to militate against its clinical use?

8. Is there an adequate margin of safety in its use?

CLINICAL OBSERVATIONS

When sufficient information regarding the experimental actions of a new drug has been obtained to permit a logical decision to be reached that clinical trial is indicated, such studies may be commenced cautiously. The primary objectives to be reached in clinical investigation are twofold: (1) to determine the therapeutic efficacy and (2) to detect all signs of clinical intolerance or toxicity. The secondary, but nevertheless important, objectives are (1) to establish the effective dosage range for different age groups and conditions, (2) to determine the type and extent of collateral treatment necessary to obtain the maximum benefit from the drug, (3) to determine the best method of minimizing any undesirable side actions incident to the use of the drug and (4) to determine the contraindications and precautions to be observed in the use of the drug. Each clinical investigator should keep these objectives clearly in mind throughout his investigation in order that nothing may be overlooked.

Frequently the pharmaceutical manufacturer concerned with the development of a new product has neither the facilities nor the personnel to investigate the drug adequately. This is particularly true of clinical investigations. This work must be undertaken by others in cooperation with the manufacturer. The selection of the investigator is important, and it is a waste of time and money and may even be dangerous to place the investigation of the safety and efficacy of a new drug in the hands of incompetent or poorly trained individuals. Furthermore, it is important to select the investigator who has proper qualifications and training in the particular phase of the problem requiring study. A good pharmacologist is not necessarily a competent pathologist; a specialist in internal medicine may not be in a position to evaluate a product offered for nasal or sinus infections. Furthermore, not all specialists in clinical medicine are capable of conducting acceptable clinical investigations. The caliber and training of each investigator should be carefully considered before putting a problem in his hands. Clinical investigation of a new drug presents many very difficult problems. The heterogeneity of the persons under observation, the difficulty of securing adequate controls, the many extraneous and uncontrollable factors, the constant presence of subjective effects influenced by conscious or unconscious bias and many other unique conditions hamper the investigator in his efforts to secure the truth. Regardless of these, it is possible to suggest certain factors to be given consideration in conducting clinical investigations:

(*a*) *The Selection of Individuals to Be Observed.*—Cooperation from subject; absence of complicating factors; age; sex; emotional and psychic factors.

(*b*) *Diagnosis.*—Objective proof of diagnosis if possible, such as isolation and identification of infecting organism; x-ray evidence or other informative laboratory data; accurate description of lesion; differential diagnosis.

(*c*) *Control Observations.*—Preliminary control observations on the individuals; concurrent observations of untreated controls; alternation of treatment; alternation of treated and control subjects; post-treatment, control observations.

(*d*) *Observation During Treatment.*—Repeated physical and laboratory examinations; hematology; urinalysis; blood chemistry; x-ray; functional tests; precise objective measurements of improvements alleged to be produced by drug; determination of concentration of drug in blood, urine and other body fluids and the correlation of levels so observed with the dosage and the effect.

(*e*) *Number of Subjects.*—Sufficient number of treated individuals to minimize chance or other uncontrollable factors from influencing results; sufficient number of untreated control subjects. The results should be subjected to statistical analysis in order to determine their reliability.

(*f*) *Carefully Planned Administration of Drug.*—Controlled variation in dosage, frequency, method and duration of administration; effect of other drugs, and so on.

(*g*) *Criteria of Benefit.*—Establishment of criteria whereby the effects of the drug may be evaluated; objective tests; subjective observations; comparison with control treatments; comparison with natural course of disease.

(*h*) *Separation of Subjective and Objective Observations.*—Use of "blind tests" (neither investigator nor subject knows which of several samples being administered is control or test product) or other methods to eliminate conscious or unconscious bias on part of observer and subject; careful separation of symptomatic reactions from objective findings; psychologic appraisal of subject.

(*i*) *Duration of Observation.*—Treatment to continue until any intrinsically undesirable or harmful manifestations have had time to develop as well as until sufficient time has elapsed to demonstrate beneficial effects; comparison of rapidity of cure or improvement with that of other methods of treatment.

(*j*) *More Than One Clinical Investigation.*—Several different investigators working independently; conclusions to be made independent of one another's results.

When the investigator is satisfied that he has a therapeutic agent which may be given satisfactorily by one route he should not by conjectural reasoning alone decide that it may be given safely and effectively by some other route. For example, if a product is safe and efficacious for oral use it may not be so when administered by rectum or by injection.

If it is decided to have several persons working on the clinical aspects of the problem, each one should provide a complete picture of the phase under investigation and not just a piecemeal study. Above all, it should be realized that summaries of case histories unless accompanied by the full report from which the summaries were derived are of little significance. A multiplicity of fragmentary case reports provide less information than a few complete and detailed reports of cases carefully and critically studied.

On completion of the clinical investigations it should be possible to provide definite answers to the questions implied in the statement of the objectives which were set forth at the beginning of this section. If these answers are not forthcoming from the data, more investigation is necessary. However, with the fulfulment of the objectives it is now necessary to decide whether the new drug has sufficient merit to be used in the alleviation of human suffering and in the treatment, prevention or cure of disease. At the same time thought should be given to providing adequate warnings against use in certain pathologic conditions or against unsafe dosage or methods or duration of administration or application.

EVALUATION OF RESULTS

Two factors enter into the decision with regard to the merits of the drug: 1. Is it efficacious? 2. Is it dangerous? Neither of these factors can be separated one from the other and considered alone. This has been emphasized by Van Winkle[6] in discussing the evaluation of new drug applications submitted under the new drug provisions of the Federal Food, Drug and Cosmetic Act. It has been emphasized that there is no arbitrary standard of safety; it is a relative matter in which the toxicity of the drug must be weighed against the therapeutic benefits which its use will bring about. Drugs with potentialities for harm and with only slight therapeutic effectiveness may be too dangerous for use, whereas another drug with the same potentialities for harm but with exceptional therapeutic usefulness may be relatively safe. Therefore, in evaluating the results of the clinical and experimental studies of a new drug, the following factors should be considered:

1. For what conditions is the drug to be offered?
2. How effective is it in these conditions?
3. Is it superior to other drugs and methods of treatment?
4. What is its inherent toxicity?
5. Does its toxicity outweigh the therapeutic advantages, keeping in mind the seriousness of the conditions for which it is being offered?
6. If there are other drugs equally or more effective in the same conditions, is the new drug less toxic or does it offer advantages in ease of administration, duration of action and so on?
7. How extensive will the use of the drug be; are its applications limited?

SUMMARY

A study of this outline for the therapeutic and toxicologic appraisal of new drugs may leave the impression that the task which has been set is far too complex and difficult, requires too much time and expenditure of energy and money and can be circumvented by briefer and less thorough investigations. While this may be true in a few isolated instances, it is not true in the majority of cases of really new drugs. Recent history contains too many instances of disastrous results that have followed incomplete or inadequate investigations on new drugs. This outline is an objective toward which investigations of new agents should be directed. It need not apply in full to all cases, but the reasons for omitting any part should be that the omitted parts of the program are not necessary and not merely that they are troublesome. It should also be borne in mind that new methods and new criteria may be developed and these should, of course, be applied when indicated.

Finally it is necessary to exercise sound judgment in deciding whether a product deserves recognition, and the only basis on which such a judgment can be made is by a careful appraisal of the data obtained through a systematic study. Investigations of new therapeutic agents are perhaps the most exacting of all scientific investigations since human health, and even life, may depend on the thoroughness of these investigations. Furthermore, failure to interpret correctly the results of the tests conducted and criteria for their evaluation may be disastrous.

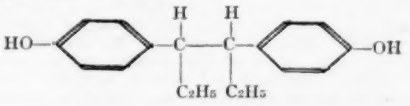
6. Van Winkle, Walton, Jr.: The Safety of New Drugs, Stanford M. Bull. 2: 103-107, 1944.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

HEXESTROL.—Meso-3,4-*di*-parahydroxyphenyl-n-hexane. $C_{18}H_{22}O_2$ (M.W. 270.36). Hexestrol may be represented by the following structural formula:



It may be prepared from anethole in ether solution by (*a*) treating with anhydrous hydrogen bromide to form anethole hydrobromide, (*b*) conversion of the anethole hydrobromide to 3,4-dianisylhexane by means of metallic magnesium, aluminum, copper or zinc turnings and (*c*) hydrolysis of the 3,4-dianisylhexane to form hexestrol. The product thus obtained may be purified by recrystallization from dilute alcohol.

Actions and Uses.—Hexestrol is used for the same conditions for which estrogenic substances are employed. It is claimed to cause a lower incidence of toxic symptoms than those which follow diethylstilbestrol administration.

Dosage.—As is the case with all estrogenic substances, the dosage of hexestrol must be adjusted to the individual case. As a guide the following dosages may be satisfactory: For menopausal symptoms, 2.0 to 3.0 mg. daily by mouth until symptoms are under control, and then 0.2 to 1.0 mg. daily as a maintenance dose; or by injection, 1.0 mg. in oil three times weekly with similar lowering for maintenance of control. For gonorreal vulvovaginitis the drug may be given orally in 3.0 mg. doses three times daily for seven days; senile vaginitis and kraurosis vulvae, 2 to 3 mg. daily by mouth, or 1 mg. in oil three times weekly by injection; suppression of lactation, 15.0 mg. one to three times daily for two or more days, or 15.0 mg. in oil daily for two or more days by injection.

Tests and Standards.—

Hexestrol occurs as an odorless white crystalline powder which melts at 185-188 C. It is freely soluble in ether; soluble in acetone, ethanol and methanol; slightly soluble in benzene and chloroform; practically insoluble in water and in dilute mineral acids. It may be dissolved in vegetable oils and in dilute solutions of sodium or potassium hydroxide. When recrystallized from diluted alcohol, hexestrol appears in the form of thin, platelike crystals of irregular, serrated outline.

Dissolve about 10 mg. of hexestrol in 10 cc. of dilute alcohol and add three drops of 1 per cent ferric chloride solution: a yellowish green color develops which changes to yellow. Add a few drops of 50 per cent solution of antimony pentachloride in dry alcohol free chloroform to a very dilute solution of hexestrol in the same solvent: a red colored solution is produced. Dissolve 10 mg. of hexestrol in 5 cc. of concentrated sulfuric acid: no color is produced (distinction from diethylstilbestrol, which yields an orange color).

The hexestrol diacetate obtained in the assay given below melts at 137-139 C.

Dry an accurately weighed specimen of hexestrol to constant weight at 100 C.: the loss does not exceed 0.5 per cent. Ignite an accurately weighed specimen of hexestrol after the addition of concentrated sulfuric acid: the sulfated ash residue is not more than 0.05 per cent. Dissolve 0.1 Gm. of hexestrol in 10 cc. of warm normal sodium hydroxide solution: the solution is clear and colorless; dilute to 20 cc. with distilled water and add 5 drops of 10 per cent sodium sulfide solution: the darkening produced does not exceed that of a control to which has been added 0.02 mg. of lead.

Transfer to a suitable flask about 0.5 Gm. of dried hexestrol, accurately weighed, and add 2 cc. of acetic anhydride and 4 cc. of dry pyridine. Boil the mixture under a reflux condenser for fifteen minutes; cool, add 50-60 cc. of distilled water and shake the flask and contents thoroughly. Stopper the flask and place it in the cold for one to one and one-half hours. Collect the precipitate on a suitable filter and wash it with four 20 cc. portions of distilled water. Dry the precipitate at 75-80 C. overnight, cool and weigh: the weight of the dry hexestrol diacetate obtained, when multiplied by 0.7628, corresponds to a hexestrol content of not less than 98.5 per cent and not more than 100.5 per cent.

LOESER LABORATORIES, INC., NEW YORK

Ampul Solution Hexestrol in Oil 1 mg. per cc.: 20 cc. Prepared with 0.5 per cent chlorobutanol.

THE WM. S. MERRELL COMPANY, CINCINNATI

Tablets Hexestrol: 0.2 mg., 1.0 mg. and 3.0 mg.

PENICILLIN (See THE JOURNAL, Oct. 7, 1944, p. 367). The following dosage form has been accepted:

SHARP & DOHME, INC., PHILADELPHIA

'Lyovac' Penicillin Sodium: 20 cc. vials containing 100,000 Oxford units.

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SATURDAY, DECEMBER 9, 1944

RESEARCH ON BRUCELLOSIS IN LATIN AMERICA

Two monographs recently published indicate that attention is being paid to brucellosis by Latin American workers. One, issued in 1942, is by Dr. M. Ruiz Castañeda,[1] the Mexican author better known for his studies on typhus fever; the authors of the other are Drs. Purriel, Risso and Espasandin from Montevideo, Uruguay.[2]

One may wonder whether after such recent and comprehensive monographs on the same subject as those by Huddleson (1940) and Harris (1941) from this country such publications were really necessary. The answer is emphatically in the affirmative. The natural tendency of the authors to emphasize the contributions of their fellow countrymen and to describe more in detail what they have themselves observed makes of their writings precious documents for the knowledge of the history and geographic distribution of a particular disease. Thus one learns from the book by Purriel and his collaborators that in Uruguay, as in England and Denmark, the melitensis variety of Brucellosis is absent whereas the abortus variety is quite prevalent, a fact explainable on account of the great prevalence of bovine over caprine herds. Morbidity for the population at large is rather low while mortality is nil. The disease in nearly all cases is of a professional type, the incidence varying in direct relation to the association of men with cattle slaughtered in the several slaughtering houses or packing houses in the republic. The infection among cattle is high, the incidence being in a direct ratio with the degree of domesticity of the animals. Milk-producing cows show 50 per cent of infection. Keeping in mind that abortion occurs at least once during the lifetime of an infected cow, and the considerable subsequent diminution in milk secretion, one will realize the economic importance of the disease in a country having a bovine population of from 7 to 8 million and where the milk of 50,000 cows is needed to supply the needs of its capital.

From Castañeda's monograph one learns that the state of affairs in Mexico is entirely different from that in Uruguay. In Mexico the vast majority of cases of human brucellosis are induced by the melitensis variety (95.2 per cent) whereas 3.5 and 1.3 per cent were induced by abortus and suis respectively. The infection in goats is suspected to be high although exact data are lacking, that of cattle varies from 25 to 50 per cent and that of swine is about 35 per cent. Human infection in Mexico is of a widespread and patchy type. Precise data are lacking, but it may be assumed that at least 3 per cent of the population has been or is infected.

The increasing social importance of brucellosis is being now realized throughout the world, and Latin American republics are not found napping in this respect. Brucellosis in Mexico and Uruguay was first demonstrated only in 1920 and 1928 respectively. Despite that, a special commission appointed by the government has been functioning in Uruguay for several years, while three medical meetings devoted exclusively to brucellosis have been held in Mexico.

Besides supplying the information on which we have commented, the monographs are valuable in several other respects. The bacteriologic, immunologic and clinical angles of the disease are exhaustively covered, valuable data are given on the choice of the best laboratory methods and new personal technics are described.

1. Ruiz Castañeda, M.: Brucelosis, Mexico, D. F., Ediciones de la Revista medicina, 1942.
2. Purriel, P.; Risso, R., and Espasandin, J.: Brucelosis: Estudio de esta enfermedad en el Uruguay, Montevideo, Editorial Independencia, 1944.

A NEW VECTOR FOR ST. LOUIS ENCEPHALITIS

The experimental transmission of the virus of St. Louis encephalitis to chickens and pigeons by nine species of mosquitoes,[1] coupled with demonstration of the virus in local Culex tarsalis during epidemic periods,[2] suggested to earlier investigators that mosquitoes are the main if not the sole insect vectors of this disease. In a survey for the presence of type specific antibodies in the human and animal populations of the St. Louis area, however, Smith[3] and her associates of Washington University School of Medicine observed that few individuals who had come into St. Louis County since 1937 showed specific antibodies, while a large percentage of the local domestic fowls approximately 1 year of age were carriers of neutralizing antibody. This suggested that some blood sucking vector that does not bite man is mainly responsible for the spread of the virus among domestic fowls.

1. Hammon, W. M., and Reeves, W. C.: J. Exper. Med. **78**: 241 (Oct.) 1943.
2. Hammon, W. M.; Reeves, W. C.; Brookman, B., and Izumi, E. J.: J. Infect. Dis. **70**: 263 (May-June) 1942.
3. Smith, Margaret G.; Blattner, R. J., and Heys, Florence M.: Science **100**: 362 (Oct. 20) 1944.

Blattner [4] had previously shown that certain ticks (Dermacentor variabilis) are capable under experimental conditions of becoming infected with the virus of St. Louis encephalitis and of transmitting it by bite to susceptible animals. Smith therefore turned her attention to the common chick mite Dermanyssus gallinae, a frequent parasite on fowls of the St. Louis area. This mite belongs to the same order of Arachnida as the tick. Its life cycle is similar to that of the tick, since both require a blood meal before molting and before egg laying by the female. Mites were therefore collected from coops in which there were 2 or more chickens whose serums contained specific neutralizing antibodies. The mites were stored in test tubes for from seven to thirty days without feeding.

In one experiment at the end of seven days' storage, 60 mites were triturated in an agate mortar in tryptose broth, and 0.1 cc. of the supernatant fluid was inoculated intraperitoneally into 11 to 19 day old Swiss mice. In a typical group 2 of the 6 inoculated mice showed signs of illness with slight twitchings or beginning convulsions on the eighth to the ninth day. These 2 mice were killed and their brains emulsified in 10 volumes of tryptose broth. After centrifugation 0.03 cc. of the resulting supernatant fluid was inoculated intracerebrally into each of 8 mice. Three days later all 8 mice developed convulsions, from which 5 died before the close of the day. From the bacteriologically sterile brains of the 3 remaining mice (now moribund) the infection was passed by the same technic to a second group of 8 mice, all of which developed convulsions by the third day.

Egg membranes inoculated with brain supernate were bacteriologically sterile but appeared slightly thick and opaque by the third day. Mice inoculated intracerebrally with a Berkefeld filtrate from such membranes developed typical convulsions by the third day. Microscopic examinations of the brains of these mice show an encephalitic process indistinguishable from the pathologic picture of St. Louis encephalitis in the mouse. Neutralization tests with specific antiserums showed that the virus in the chick mite is qualitatively identical with the standard laboratory strain of the virus of St. Louis encephalitis originally isolated from a human case.

Blattner [4] found that ticks infected with encephalitis can transmit the virus to their offspring for innumerable generations. Assuming that a similar hereditary transmission of the virus takes place in infected mites, Smith concludes that infected mites may well account for the permanence of the viral infection in domestic fowls of the St. Louis area. From these fowls sporadic human cases of mosquito borne encephalitis might readily occur. Recognition of the mite as an interfowl vector, therefore, may well lead to practical methods of reducing the number of sporadic human cases.

4. Blattner, R. J., and Heys, Florence M.: J. Exper. Med. **79**: 439 (April) 1944.

CONGENITAL MALFORMATIONS

The embryologic explanation of a common congenital malformation, even if known, is often not readily accessible to the pathologist or surgeon. Three recent important contributions to early human embryology have just been reported by Bremer of Harvard.

The first of the series,[1] on the embryology of congenital aneurysms of the cerebral arteries, was the outcome of interest inspired by the untimely death of Dr. Soma Weiss. Two types of congenital aneurysms of the cerebral arteries are described by Bremer and their origin is traced. The first type he ascribes to the consequence of the rapid growth of the cerebral hemisphere during fetal life, which spreads the forks of the branches of the cerebral arteries which approach from the lesser curvature of the expanding hemisphere. If the forks of these branches of the cerebral arteries should lack media, the rapid spread may cause local aneurysms. The second cause Bremer found to be enlargement of the proximal portion of the plexuses formed from branches of the cerebral arteries which dip into the brain substance. If the enlargement persists while the distal communications degenerate, aneurysmal pouches from the main vessels may be formed.

The second paper,[2] on the diaphragm and diaphragmatic hernias, was the outcome of Dr. Bremer's attendance at clinical pathologic conferences at the Children's Hospital, Boston. This important contribution to its embryology opens with a detailed consideration of the development of the diaphragm . . . "of which there is, to my mind, no adequate description."

The defects of the diaphragm are divided into several groups. The first is concerned with the last step in the development of the membranous portion: fusion of the two sets of diaphragmatic muscles (costal and lumbar) peeled off the body wall. Irregularities in the growth of pleuroperitoneal membrane produce a hernia recognized by its position lateral to the dorsal lobe of the liver; failure of the normal cutting off by the crural muscles of the infracardiac bursa may leave an open communication from the superior recess of the lesser peritoneal cavity into the right pulmonary ligament. These are true congenital hernias. Through additions to our knowledge of the development of the diaphragm, Bremer has completely classified the nature of its congenital defects and has provided an accurate nomenclature to replace the confusion so often characterizing discussions concerning hernias of the diaphragm.

The third paper,[3] on anomalies of the intestinal tract, "duplication" or "reduplications," "enteric cysts" or "enterogenic cysts," "ileum duplex" and "giant diverticula," is also the result of investigations inspired by attendance at clinical pathologic conferences. Bremer divides these abnormalities of the intestinal tract into

1. Bremer, J. L.: Congenital Aneurysms of the Cerebral Arteries: An Embryologic Study, Arch. Path. **35**: 819 (June) 1943.
2. Bremer, J. L.: The Diaphragm and Diaphragmatic Hernia, Arch. Path. **36**: 539 (Dec.) 1943.
3. Bremer, J. L.: Diverticula and Duplications of the Intestinal Tract, Arch. Path. **38**: 132 (Sept.) 1944.

two groups on the basis of embryologic origin. Most of the spherical cysts are derived from true diverticula, which are found frequently on the antimesenteric surface of the intestine in embryos of eight to nine weeks. When normal absorption of these diverticula does not take place they may continue to grow and so bulge within the lumen, if restricted by muscle layers, or expand outside the bowel if the muscle wall is pierced. In the second group are a few spherical and most of the tubular "cysts," and these Bremer regards as true duplications. These originate by an abnormal persistence of the vacuoles among the massed cells or "solid stage" of the intestine, a phenomenon found under normal conditions in the embryo of six to seven weeks. By confluence of a chain of vacuoles a new channel is formed parallel to the original lumen. The intestinal layers grow between the two. These duplications, which contain all the layers of the normal intestine, lie usually between the leaves of the mesentery. They may be isolated and cystic, or they may communicate with the parent lumen. A study of the structure and origin of these duplications makes clear why it is impossible in most instances to remove the duplication without resecting the adjacent bowel.

The direction of Bremer's research activities in the freedom following academic retirement has been influenced by his realization of the kinds of knowledge most in current demand by pathologists and clinicians. These important advances in embryology have immediate practical application.

Current Comment

CELLULAR TRANSFORMATION

Under the influence of carcinogenic agents normal cells may be changed into cancer cells with the power of autonomous growth. This change is permanent and inheritable. So far no way has been found to turn cancer cells back into normal cells; hence success in the treatment of cancer depends on the removal or destruction of the cancer. Are there examples in biology of more or less similar cellular transformations? The answer is yes. In his instructive review of the mechanisms of cell transformations Haddow [1] discusses irreversible and inheritable mutations studied recently by different investigators in plants, in Paramecium aurelium, in tumor producing viruses and in pneumococci. The interconversion of specific pneumococcus types was first described by Griffith.[2] Now Avery and his co-workers [3] have found that the transforming agent is a thymonucleic acid—a discovery of far reaching implications in biology. "Once transformation has occurred," writes Haddow, "the newly acquired characteristics are thereafter transmitted without any further addition of the transforming agent." In other words, a change has taken place in the pneumococcus cells much like that in normal cells when transformed into cancer cells. Haddow concludes by pointing out that relationships like those mentioned "seem more than mere analogies and strongly suggest an underlying unity of principle in the growth and differentiation of organisms of the most highly diverse kinds."

1. Haddow, A.: Transformation of Cells and Viruses, Nature **154**: 194 (Aug. 12) 1944.
2. Griffith, F. J.: J. Hyg. **27**: 113, 1928.
3. Avery, O. T.; MacLeod, C. M., and McCaskey, M.: Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types, J. Exper. Med. **79**: 137 (Feb.) 1944.

PROGRESS IN THE TREATMENT OF TYPHUS FEVER AND OF ROCKY MOUNTAIN SPOTTED FEVER

The conditions caused by specific rickettsias, such as typhus and Rocky Mountain spotted fever, present striking etiologic, pathologic and clinical similarities. The course and the symptoms result largely from the widespread localization of the rickettsial organisms in the vascular endothelium. In a detailed study of the circulation in severe epidemic typhus in French Morocco Woodward and Bland [1] obtained evidence that circulatory collapse in typhus is mainly peripheral in origin and not due to primary cardiac failure. They demonstrated reductions in the blood volume and in blood proteins, especially albumin, and other alterations, all of which are explainable as due to the vascular lesions of typhus and increased capillary permeability. Emphasis is placed on the importance of general supportive measures to restore the volume and the quality of the blood. Harrell and his co-workers [2] have pointed out that supportive measures are not used as much as they should be in the treatment of Rocky Mountain spotted fever. They too emphasize the loss of volume and of proteins by the blood on account of the vascular lesions which may lead to peripheral circulatory collapse if the proper treatment is not given. Yeomans and others [3] have reported on the effect of para-aminobenzoic acid in epidemic typhus in Cairo, Egypt. Under well controlled conditions they compared the clinical course of 20 treated cases with that of 44 control cases. Beginning with 4 to 8 Gm. of para-aminobenzoic acid by mouth, 2 Gm. was given every two hours or enough to maintain the concentration of the acid in the blood between 10 and 20 mg. per hundred cubic centimeters until the rectal temperature remained at 99.5 F. or less for twenty-four hours. These amounts were taken with ease by the patients and without any serious untoward effects. In patients who received the acid in the first week of illness the course of the attack was much less severe and considerably shorter than in "untreated" patients. The fact that para-aminobenzoic acid may have curative effect in human as well as in mice typhus [3] directs attention to many problems for investigation. What effect will para-aminobenzoic acid and related compounds have on Rocky Mountain spotted fever and other rickettsial diseases?

1. Woodward, T. E., in collaboration with Bland, E. F.: Clinical Observations in Typhus Fever, with Special Reference to the Cardiovascular System, J. A. M. A. **126**: 287 (Sept. 30) 1944.
2. Harrell, G. T.; Venning, William, and Wolff, W. A.: The Treatment of Rocky Mountain Spotted Fever, this issue, p. 929.
3. Yeomans, Andrew; Snyder, J. C.; Murray, E. S.; Zarafonetis, C. J. D., and Ecke, R. S.: The Therapeutic Effect of Para-Aminobenzoic Acid in Louse Borne Typhus Fever, J. A. M. A. **126**: 349 (Oct. 7) 1944.

MEDICINE AND THE WAR

ARMY

QUARANTINE BRANCH ESTABLISHED IN PREVENTIVE MEDICINE SERVICE

A quarantine branch, under the direction of Lieut. Col. Phillip T. Knies and in cooperation with the U. S. Public Health Service and the Navy, has been established in the Preventive Medicine Service of the Surgeon General's Office, to afford all possible protection against diseases and harmful pests which might be brought from foreign countries by military traffic. The new Army quarantine policy takes advantage of the Army immunization program and of the constant medical supervision of the soldier. Modern methods of immunization, it was stressed by the Surgeon General, offer great advantages from the standpoint of preventing the introduction of diseases into this country as well as protecting the health of the soldier. Army personnel routinely receive immunizations for smallpox, typhoid and paratyphoid fever and tetanus. Special immunizations are given, in accordance with instructions from the Surgeon General, for typhus, yellow fever, cholera and plague. The Army program also includes measures to prevent the importation of dangerous insects from abroad. Extensive insect control programs have been carried out about military stations and airports abroad, using the highly effective technics and agents which have been developed.

Future developments in the field of quarantine will include greatly improved methods for the international notification of disease, along with improved health certification of travelers so that officials at ports of entry will have the necessary medical data for accurate judgment with the least possible delay to travelers. The extensive military program now being developed is expected to go far in demonstrating the value of new methods growing out of wartime medical progress.

BRIGADIER GENERAL JAMES S. SIMMONS AWARDED WALTER REED MEDAL

The Walter Reed Medal was recently presented to Brig. Gen. James S. Simmons, chief of the Preventive Medicine Service, in recognition of meritorious achievement in tropical medicine. The Walter Reed Medal was established by the American Society of Tropical Medicine in 1934 to be awarded periodically in recognition of meritorious achievement in tropical medicine by an individual or an institution. The first award was made at the thirty-second annual meeting of the society in 1936, at which time one medal was presented to the widow of Walter Reed, and one was awarded to the Rockefeller Foundation for its study and control of yellow fever. In 1939 the award was made to Dr. William B. Castle of Harvard University, in 1940 to Dr. Herbert Clark of the Gorgas Memorial Laboratory in Panama and in 1942 to the United States of Brazil "for outstanding work in the eradication of Anopheles gambiae in Brazil" and posthumously to Dr. Carlos J. Findlay of Havana, Cuba.

HONOR DEAD OF SECOND A. E. F. DIVISION

Armistice day ceremonies, sponsored by the Second Division, A. E. F. Association, were held at the Second Division monument (17th Street and Constitution Avenue), Washington, D. C., to commemorate the attack launched on June 6, 1918 by the Second A. E. F. Division, which saved Paris and paved the way for the march to the Rhine. The fourth brigade of the division, made up of Marines, Navy physicians, dentists, hospital corpsmen and chaplains, spearheaded the attack against the Germans at Belleau Wood.

Veterans of the Second A. E. F. Division, composed of Army, Navy and Marine Corps units, are now serving as officers of the fifth and sixth regiments, which fought at Guadalcanal, Tarawa, Saipan and elsewhere. The ninth and twenty-third regiments, Second Division, U. S. Army, also officered by Second A. E. F. Division men, fought in Normandy and are still in action in Europe.

Rear Admiral Alexander C. Lyle (DC), U.S.N., winner of the Congressional Medal of Honor in the first world war while serving with the Fifth Marines, Second Division, A. E. F., represented Vice Admiral Ross T. McIntire, Surgeon General of the Navy, at the Armistice day ceremonies. Major Gen. Dewitt Peck, assistant commandant of the U. S. Marine Corps, spoke in behalf of the veterans of the three services who comprised the Second Division, the first combined unit under a single command in American military history.

GENERAL LULL ADDRESSES GRAY LADIES

Speaking recently before the first graduation class of the hospital course for Gray Ladies, held at the station hospital at Fort Belvoir, Virginia, Major Gen. George F. Lull, Deputy Surgeon General, emphasized the important relationship between hospital personnel and the sick soldier, with special reference to the soldier returning from overseas. The Gray Ladies constitute a Red Cross volunteer organization that perform various services for hospitalized men in the armed forces.

ARMY AWARDS AND COMMENDATIONS

Major Lloyd W. Taylor

Major Lloyd W. Taylor, formerly of Washington, D. C., has been awarded the Legion of Merit by Major Gen. James L. Frink, commanding general of the U. S. Army Services of Supply in the Southwest Pacific. The honor was bestowed on Dr. Taylor for his work in late 1942 and early 1943 as supply officer of a medical unit serving combat troops in New Guinea. Suffering from illness and fatigue, Dr. Taylor obtained badly needed medical supplies for American and Australian hospitals other than his own, in addition to doing his regular work caring for wounded men. He is now assigned to the Office of Chief Surgeon of the Southwest Pacific area, helping in the evacuation of patients from battle zones to Australia and the United States. Dr. Taylor graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1941 and entered the service June 1, 1942.

Lieutenant Colonel Willis B. Johnson

Lieut. Col. Willis B. Johnson, formerly of Everett, Wash., was recently presented the Bronze Star Medal. The citation accompanying the award read "From July 30 to Aug. 28, 1943 at New Georgia, British Solomon Islands, he was in command of a medical battalion which moved from Guadalcanal into close support positions on New Georgia under enemy air and ground attacks. The effective evacuation and field treatment of casualties under the most trying conditions of terrain and weather during this operation were largely due to his high professional and military knowledge as well as his determination." Dr. Johnson graduated from the College of Medical Evangelists, Loma Linda-Los Angeles, in 1937 and entered the service Sept. 16, 1940.

Captain Mark W. Dick

The Bronze Star Medal was recently awarded to Capt. Mark W. Dick, formerly of Grand Rapids, Mich. His citation read "On March 12, 1944, at Bougainville, Solomon Islands, while enemy mortar shells exploded around him, he ran 40 yards and crawled under a barbed wire entanglement

to reach a seriously wounded soldier. Finding that the nature of the man's wounds made it impossible to move him to the protection of a pillbox, he unhesitatingly exposed himself and stood in an upright position to administer medical treatment during the intense mortar barrage." Dr. Dick graduated from the University of Michigan Medical School, Ann Arbor, in 1932 and entered the service May 6, 1942.

Captain Richard D. Roys

Capt. Richard D. Roys, formerly of Seattle and now a company commander of a medical unit on an island north of New Guinea, has been decorated with the Bronze Star for bravery in caring for the wounded under fire. Dr. Roys already held the Silver Star, awarded for bravery in action in New Guinea last year. He graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1939 and entered the service Nov. 14, 1940.

Colonel Benjamin M. Baker

Col. Benjamin M. Baker, formerly of Baltimore, has recently been awarded the Legion of Merit by General Douglas B. MacArthur for "exceptionally meritorious conduct in the performance of outstanding services in the South Pacific Area from April 20, 1942 to June 13, 1944." Dr. Baker graduated from Johns Hopkins University School of Medicine, Baltimore, in 1927 and entered the service in 1940.

Captain Salvatore L. Pernice

The Bronze Star Medal for meritorious service in the Solomon Islands was awarded recently to Capt. Salvatore L. Pernice, formerly of Brooklyn. Dr. Pernice was cited for his work in accompanying tanks into combat in order to study problems concerned with the evacuation of casualties from tanks. Dr. Pernice graduated from Long Island College of Medicine, Brooklyn, in 1928 and entered the service June 18, 1942.

Lieutenant Colonel Byron B. Cochrane

The following citation was recently conferred on Lieut. Col. Byron B. Cochrane, formerly of St. Paul, previous to his promotion to that rank: "For meritorious service in connection with military operations against the enemy from Jan. 30 to Feb. 8, 1944. During the training stages for the Kwajalein operation Major Cochrane devised new and ingenious methods for the treatment and evacuation of casualties. His untiring effort and devotion to duty resulted in a superior organization prepared to handle all casualties in the most efficient manner. During constantly changing situations and numerous attacks he displayed great zeal and initiative, which inspired his officers and men to greater effort in the treatment of the wounded. In order that he might properly supervise and carry out his duties, Major Cochrane made numerous trips to the front lines with complete disregard for his own safety. His resourcefulness made possible the immediate treatment and evacuation of the wounded, thus saving the lives of many who would otherwise have died." Dr. Cochrane graduated from the University of Minnesota Medical School, Minneapolis, in 1938 and entered the service in February 1942.

Captain Willard E. Goodwin

The Soldier's Medal was recently awarded to Capt. Willard E. Goodwin, formerly of Baltimore. The citation read "He rescued an army nurse from a rough sea after she had been swept into a gorge on Feb. 27, 1944 at New Zealand. He went to the aid of the helpless nurse, who was being dragged against the rocks and had suffered painful injuries. Succeeding in swimming to her, he assisted her out of the gorge to a sandy beach some 400 yards away. His prompt action was responsible for saving her life." Dr. Goodwin graduated from Tufts College Medical School, Boston, in 1941 and entered the service after completing his internship in 1942.

Captain Jarvis M. Hyatt

Capt. Jarvis M. Hyatt, formerly of Dearborn, Mich., has been awarded the Bronze Star Medal for meritorious service and disregard for his own personal safety in France on Aug. 18 and 19, 1944 in connection with military operations against an enemy of the United States. Dr. Hyatt graduated from Wayne University College of Medicine, Detroit, in 1936 and entered the service Aug. 13, 1942.

Captain Weldon T. Ross

Capt. Weldon T. Ross, formerly of McMinnville, Ore., has been awarded the Legion of Merit in the European theater of operations for "exceptionally meritorious conduct in the performance of outstanding services from Sept. 10 to Oct. 20, 1943." Dr. Ross graduated from Duke University School of Medicine, Durham, in 1938 and entered the service in 1941.

NAVY

GORGAS MEDAL AWARDED TO COMMANDER JAMES J. SAPERO

The Gorgas Medal, established in memory of Surgeon General William Crawford Gorgas in 1942 and sponsored by Wyeth, Incorporated, Philadelphia, was awarded this year to Comdr. James J. Sapero for distinguished service as an officer of the Medical Corps, United States Navy. The presentation was made by Frank F. Law, vice president of Wyeth, Incorporated, at the annual dinner of the Association of Military Surgeons, held at the Hotel Pennsylvania, New York, November 3. Rear Admiral Harold V. Smith, chief of the Research Division Bureau of Medicine and Surgery, U. S. Navy, acted as proxy for Commander Sapero.

The Gorgas Medal in 1942 in a threefold award went to Rear Admiral Edward R. Stitt of the Navy Medical Corps and Brig. Gens. Frederick F. Russell of Boston and Jefferson R. Keen, former army surgeons. In 1943 the medal was awarded to Dr. Hugh Smith Cumming, surgeon general, United States Public Health Service, retired.

NAVY NURSE RECEIVES MEDAL

Lieut. Comdr. Mary Martha Heck, Nurse Corps, U. S. N., who recently completed a tour of duty as officer in charge of the contingent of Navy Nurses in England, was awarded the Bronze Star Medal for "meritorious service" and "untiring effort." The presentation was made by Admiral Harold R. Stark, commander, Naval Forces in Europe.

FIRST WHOLE BLOOD BANK ABOARD SHIP

In the past the distances that lay between advanced bases and new combat areas had eliminated the transporation of whole blood by sea. With this knowledge Capt. John T. Bennett, United States Navy Medical Corps, Hattiesburg, Miss., made a decision that was to save many lives. That decision created the first known blood bank to be water borne to the fighting front aboard a hospital ship. Success of this experiment depended on the ability of living blood to survive disturbances created by vibrating ship's engines and the rolling and pitching of the ship. It was known that ashore, under proper conditions, whole blood could be kept as long as ten days. With the decision made, the commanding officer of shore garrisoned Marines at an advanced base in the Marshall Islands, where the ship lay at anchor, was consulted. The medical officer asked for 100 volunteers. Over 300 men from the small marine garrison responded. One hundred were selected, came aboard, gave their blood and assured a rich, floating blood bank. The following morning the ship was under way with her precious cargo and anxious hopes for the success of the experiment. The success of their efforts can now be seen. American fighting men who came aboard seriously wounded took the road to recovery. At Guam there was ample whole blood for required transfusions. No wounded fighting man went without whole blood if it was required.

NAVY AWARDS AND COMMENDATIONS

Captain Harry L. Goff

An award of the Bronze Star Medal was recently conferred on Capt. Harry L. Goff, formerly of Pembroke, Ga., "for meritorious performance of outstanding services as medical officer on the staff of the commander of an amphibious force in both the preparation and the execution of the amphibious assault on the coast of France, June 6, 1944. Captain Goff was charged with the organization and training of medical staffs and the evacuation and care of both Army and Navy casualties during the assault. The high level of efficiency maintained in this service was due to Captain Goff's able planning and resourcefulness and contributed in a substantial manner to the success of the operation. The sound judgment, initiative and devotion to duty displayed by Captain Goff on this occasion reflect great credit on the United States Naval Service." Dr. Goff graduated from Jefferson Medical College of Philadelphia in 1925 and entered the service June 8, 1925.

Lieutenant Joseph John Connor

The Bronze Star Medal was recently awarded to Lieut. Joseph J. Connor, formerly of Denver, for service as set forth in the following citation: "For meritorious service as medical officer attached to Boat Pool Eleven operating in the Solomon Islands Area on Nov. 29, 1943. Assigned the hazardous mission of accompanying a boat pool during the evacuation of a Marine battalion from a position several miles behind Japanese lines, Lieutenant Connor worked tirelessly in caring for the injured despite a constant barrage of enemy machine gun, mortar and artillery fire. Although forced to work in complete darkness, he carried out his task so skilfully and with such exceptional efficiency that no lives were lost. Lieutenant Connor's cool courage under fire and his heroic devotion to duty in the face of grave peril contributed to the saving of many lives, and his gallant conduct throughout the operation was in keeping with the highest traditions of the United States Naval Service." Dr. Connor graduated from the University of Colorado School of Medicine, Denver, in 1941 and entered the service in July 1942.

MISCELLANEOUS

BRITISH WOMAN ARMY DOCTOR HONORED

Lieut. Col. Albertine Winner, R. A. M. C., director of the Woman's Medical Services of the British army, was guest of honor at a dinner given recently by Major Gen. Norman T. Kirk, Surgeon General of the Army. Major Gen. George F. Lull, Deputy Surgeon General, acted as toastmaster. Colonel Winner spoke on the work of the British women in the British army, and Major Margaret Janeway, Office of the Surgeon General, talked on the activities of women in the Medical Department of the Army of the United States.

Colonel Winner's visit to this country included the annual meeting of the Association of Military Surgeons and an inspection tour of various WAC installations.

GERMANS TOLD TO EXPECT FURTHER FOOD RESTRICTIONS

According to a dispatch in the Stockholms *Tidningen* reported recently by the Office of War Information, the German food ministry has stated that another reduction in bread, fat and sugar rations in Germany is imminent because the total supply had declined by one fifth since the loss of the "eastern territories." It was also stated that livestock had already decreased to such an extent "that to increase meat rations as a substitute for reduced bread and fat rations was no longer feasible." One fourth of the entire German potato crop this year is needed for the manufacture of fuel, and 3,000,000 tons of sugar beets is necessary for making industrial alcohol, the dispatch also reported.

German weekly bread rations, already low, were scheduled to be cut by 7 ounces per person because of "decreased imports" and a poor grain harvest, according to a recent Nazi DNB agency dispatch to the German press. Normal consumers were to get 78 ounces a week, or less than three quarters of a pound per day of the basic food staple.

NEW HOSPITAL CAR FOR USE IN THE UNITED STATES

The first of a new type hospital car for use in the United States was opened for inspection in Washington, D. C., recently. These new unit type cars are not converted pullmans but are designed and built as hospital cars. They are 10 feet longer, are air conditioned and accommodate 38 patients and attendant personnel. Each includes two rows of triple tiered beds, two compartments with 3 beds each, a stainless steel kitchen equipped with refrigeration, ice cream cabinet and coal range, a receiving room with 4 foot side doors for loading and unloading litter patients, two roomettes each with toilet and shower for the medical staff or seriously ill patients, and a baggage compartment. The car also carries a modern pharmacy unit and sterilizing equipment, and in case of emergency either the receiving room or one of the roomettes can be converted quickly into an operating room. The Glennon type, steel frame beds are adjustable, and unoccupied center bunks can be dropped to provide seating accommodations for ambulatory patients.

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

Mayo General Hospital, Galesburg, Ill.: Diseases of the Intestinal Tract—Medical and Surgical Diagnosis and Care, Drs. Warren H. Cole and Michael H. Streicher, December 13.

Camp Ellis, Illinois: Malignancies in the Army Age Group—Medical X-Ray and Surgical Diagnosis and Treatment, Drs. George J. Rukstinat and Alexander Brunschwig, December 13.

Chanute Field, Rantoul, Ill.: Bone and Joint Infections, Dr. Cly Howard Hatcher and Lieut. Col. Ralph Soto-Hall, December 13.

Vaughan General Hospital, Maywood, Ill.: Dermatologic Diseases, Drs. Francis E. Senear and James H. Mitchell, December 13.

Fort Sheridan, Illinois: Conditions Affecting Glucose Metabolism, Dr. Arthur R. Colwell, December 13.

Percy Jones General and Convalescent Hospital, Battle Creek, Mich.: Symposium on Convulsive Disorders: Psychiatric Approach, Major I. L. Turow; Neurosurgical Approach, Major Frank H. Mayfield; Neurologic Approach, Lieut. D. B. Foster, December 18.

U. S. Naval Hospital, Philadelphia: The Epileptic Personality, Dr. Harold Palmer, December 29.

HOSPITALS NEEDING INTERNS AND RESIDENTS

The following hospitals have indicated to the Council on Medical Education and Hospitals that they have not completed their house staff quota allotted by the Procurement and Assignment Service:

(Continuation of list in THE JOURNAL, December 2, page 903)

CALIFORNIA

Permanente Foundation Hospital, Oakland. Capacity, 134; admissions, 3,693. Sidney R. Garfield, Medical Superintendent (interns, July 1945).

KANSAS

St. Francis Hospital, Wichita. Capacity, 450; admissions, 13,721. Sister M. Oswaldine, R.N., Superintendent (2 interns, 1 now, 1 Jan. 15, 1945).

NEW YORK

Our Lady of Victory Hospital, Lackawanna. Capacity, 185; admissions, 4,143. Sister M. Bathilde, Superintendent (interns).

Crouse-Irving Hospital, Syracuse. Capacity, 245; admissions, 7,035. Miss Dorothy Pellenz, Assistant Superintendent (3 interns).

VIRGINIA

Riverside Hospital, Newport News. Capacity, 233; admissions, 5,578. Arthur H. Perkins, Medical Superintendent (1 resident—mixed).

ORGANIZATION SECTION

Council on Medical Service and Public Relations

Meeting Held in Cincinnati

Representatives of the Medical Societies of Ohio, Kentucky, Indiana and West Virginia met in Cincinnati, October 29, in response to an invitation from Dr. E. J. McCormick, a member of the Council on Medical Service and Public Relations.

Mr. J. W. Holloway, Acting Secretary of the Council, stated the program and activities of the Council, as encompassed in the six directives from the House of Delegates. Namely:

1. To make available facts, data and medical opinions with respect to timely and adequate rendition of medical care to the American people.
2. To inform constituent associations and component societies of proposed changes affecting medical care in the nation.
3. To inform constituent associations and component societies regarding the activities of the Council.
4. To investigate matters pertaining to the economic, social and similar aspects of medical care for all the people.
5. To study and suggest means for the distribution of medical service to the public consistent with the principles adopted by the House of Delegates.
6. To develop and assist committees on medical service and public relations originating within the constituent associations and component societies of the American Medical Association.

Dr. Joseph S. Lawrence, director of the Washington office, was asked to outline the program of the Washington bureau which the Council is sponsoring. He said that the objective of the Washington bureau was not to be a lobby or to conduct a lobby but rather to be a center of information through which the states might receive information concerning actions of Congress and of government bureaus. He hopes that the relationship can be so streamlined that each state will, through its appointed representatives, at all times be thoroughly informed with what is transpiring in Washington. He called attention to a series of hearings that Senator Pepper, chairman of the Senate Subcommittee on the Nation's Wartime Health Program, is holding. Printed copies of the proceedings of two (parts 2 and 5) of these hearings are available and contain exceedingly valuable information. It was recommended that each physician write to his Congressmen requesting a copy of each. The Washington office will expect each of the state societies to discuss matters that are reported from Washington with its Congressmen.

Dr. Lawrence urged physicians to give careful thought to legislation in order that there may be unanimity of opinion in the Association. Physicians have the reputation of not being able to agree, and Congressmen are inclined to take advantage of this divergence of opinion when it is to their interests. If we as an association are united in opinion we shall be able to effect an influence which cannot be ignored.

The question arose as to how the Council should determine what instructions to give the Washington office on pending legislation and whether the opinion should arise with the states or with the Council. A vote was taken which indicated that it was the sense of those present that the Council should decide whether or not legislation is inimical and that information should be passed on to the states, which would then support such action as the Council outlined.

Dr. James R. Bloss of the Board of Trustees urged the members to pay more attention to the reports in THE JOURNAL of the Association's various activities. He stated that the Board of Trustees is heartily supporting the Council. Inquiry of the physicians in service, he reported, showed conclusively that they will seek postgraduate opportunities when they are out of the service.

Dr. L. Howard Schriver, president of the Ohio society, confessed that the conference put him in an optimistic frame of mind. He thought it an especially good sign that the American Medical Association had taken this advanced step of learning more intimately the feelings and opinions of its members. In his opinion the profession has been too passive, too academic. We should take a more active interest in social politics and teach our students to do so.

Dr. Elmer L. Henderson, a Trustee, replied to a complaint made by one of the physicians that communications directed to the Board of Trustees were not answered promptly and explained that the Trustees are not in continuous meeting and so delays should not be interpreted as showing a lack of interest. The board is a hard working body and gives consideration to every suggestion that is submitted.

Dr. Jonathan Forman of Ohio urged that special effort be taken to educate the public in health matters. The people want to be informed on the health conditions of their communities. More knowledge would obviate much muddled thinking and increase a desire for good health.

Dr. A. A. Brindley reported that a prepayment plan of insurance began functioning in Toledo on July 1, 1944 and in the first four months over 6,100 contracts were written, 38 per cent on an employee only basis, 19 per cent on the employee and one dependent basis and 43 per cent on the family basis. The total number of people covered is 15,347. Thus far 473 claims have been paid. Maternal care is not included in the plan.

Dr. R. L. Sensenich, a Trustee, called attention to the pamphlet on medical service prepared by the Bureau of Medical Economics, describing many sickness insurance plans now operating. Obviously no one person is wise enough to draft a plan for the whole United States that would be just the plan to fit any particular county or community. Large insurance companies are still experimenting with their problems. The states which have tried to establish insurance plans have met with varying degrees of success and failure. Before a plan can succeed there must be unanimity of opinion as to the type of plan wanted.

Dr. Barney J. Hein made a strong appeal for unanimity and then for leadership.

Dr. Robert E. S. Young of Columbus reported briefly on studies he has made of sickness insurance plans and of the philosophy back of them. He pointed out that government plans have a great political value; even industry finds other use for the power it gets in controlling its private plan than that of providing medical care. This control can be modified by the physicians if they unite to preserve their rights and study sympathetically the problems involved in developing a plan.

Dr. W. H. Howard reported on the plan Indiana is studying. Two sets of conditions present themselves: Should the plan be administered by the physicians or by an insurance company? Should it be on a service or on an indemnity basis?

At the close of the conference, late in the afternoon, many expressed themselves as feeling that the success of this conference justified the Council's efforts and as hoping that there will be other conferences in the future.

Society Proceedings

COMING MEETINGS

American Academy of Orthopaedic Surgeons, Chicago, January 21-24. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

American Society of Anesthetists, New York, Dec. 14. Dr. McKinnie L. Phelps, 745 Fifth Ave., New York 22, Secretary.

Annual Forum on Allergy, Pittsburgh, January 20-21. Dr. Jonathan Forman, 956 Bryden Road, Columbus, Ohio, Director.

Association for Research in Nervous and Mental Diseases, New York, Dec. 15-16. Dr. Thomas E. Bamford Jr., 115 E. 82d St., New York 28, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 15-17. Dr. E. Martinez-Rivera, P. O. Box 3866, Santurce, Secretary.

Society of Surgeons of New Jersey, Jersey City, January 31. Dr. Walter B. Mount, 21 Plymouth St., Montclair, N. J., Secretary.

Washington Letter

(From a Special Correspondent)

Dec. 4, 1944.

Labor Plans Social Security Legislation

Plans of the two major labor unions with regard to the Wagner-Murray-Dingell bills now pending in Congress, which provide "everything in social security, including the kitchen sink," are to split the bills into four or five separate proposals, to replace the omnibus measure, according to union spokesmen. These plans, of course, have yet to be cleared with Congressmen who have the say in the matter.

The extension of old age and survivors' insurance to the "missing 20 million" not now covered by social security would be put up to Congress in a separate bill from others dealing with such controversial questions as "socialized medicine" and federalization of state unemployment insurance systems. The Wagner-Murray-Dingell bills have been in Congressional committees for a year and a half without hearings. It is believed that favorable action can be obtained on parts of the bills by divorcing them from the proposals which aroused strong group opposition.

Civil Services Hire Disabled Vets Quickly

Dr. Verne K. Harvey, medical director of the Civil Service Commission, revealed to the House Committee to Investigate Aid to the Physically Handicapped that Civil Service is now prepared to place disabled veterans in government jobs quickly and effectively. This was accomplished through analyses of 41,823 handicapped persons placed in government jobs since Oct. 1, 1942 and study of thousands of jobs. Duties are classified to the point where it has been determined how many fingers will be required for specific jobs. Positions have been listed which can use persons who have disabilities in arms, legs, vision and hearing. Dr. Harvey said that much had been done through the Coordinating Committee for the Placement of the Physically Handicapped, a joint committee representing the Civil Service Commission, Federal Security Agency, Council of Personnel Administration, Veterans Administration and the Veterans Employment Service.

Maryland and District in Licensing Squabble

Action of the Maryland Board of Medical Examiners in refusing to grant a Washington doctor a $1 "borderline" certificate entitling District of Columbia physicians to practice in nearby Maryland has precipitated a controversy here. The District Commission of Licensures may retaliate December 11 by revoking $1 "courtesy" certificates entitling Maryland doctors to practice in the Capital. Dr. George C. Ruhland of the District health office and the executive board of the District Medical Society have criticized the action of the Maryland board at a time when there is reported to be a grave shortage of licensed physicians in adjacent Prince Georges and Montgomery counties of Maryland.

Mrs. Roosevelt Praises Epidemic Control

The notable achievement of the American medical profession in keeping down epidemics during this war was mentioned by Mrs. Roosevelt in her address at Pan American Health Day ceremonies here December 2. "In this war," she said, "a remarkable thing has been achieved in keeping us from epidemics which might have taken a heavy toll." By comparison, she recalled the influenza epidemic of the last war, which cost many lives and slowed up the war effort not only in this country but also in others.

Dr. L. S. Rowe, director general of the Pan American Union, said that scientific estimates showed that further health protection throughout the Americas would increase production by more than 30 per cent. Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service, said that a permanent international health organization after the war is essential. Among its possible functions, he said, would be collection and interchange of epidemic intelligence, standardization of biologic products including international standards of food and drugs, international action to train public health personnel through establishment of international schools of hygiene, commissions of experts to promote control of major diseases, health education, and scientific guidance on nutritional policies.

Charles M. Hay, deputy chairman and executive director, War Manpower Commission, assured delegates from other nations that all facilities of the United States would be available to carry out an international health program. Among Latin American speakers were Julian R. Caceres, Honduras, and Ambassador Don Pedro Beltran, Peru.

1944 Version of Townsend Plan Considered

Near the stage where it will be debated in the House is the "1944 version of the Townsend old age pension plan," a bill sponsored by Representative Pat Cannon, Democrat, of Florida. It differs from the Townsend plan in that it would levy a 3 per cent tax on the gross income of every individual and business, with $100 monthly exemption for personal incomes. Under the earlier plan a 2 per cent tax on every business transaction except payment of wages or salaries was to provide the money. Later a 2 per cent tax on wages, inheritances and gifts and a 10 per cent increase in income tax were added. The old Townsend plan set a maximum pension of $200 a month, but the Cannon bill does not specify the amount. Eligible for pensions under the Cannon measure would be all over 60, disabled under 60 and mothers taking care of children under 18. Pensioners would not hold jobs and would have to spend every monthly check within thirty days. Economists pointed out that $200 a month for around 12,000,000 pensioners would cost close to $35,000,000,000 a year and that taxes would increase retail prices and the cost of living.

Army Prepares for Heavy Casualties

The Army is anticipating a steady increase in casualties from overseas and is trying to provide a maximum of bed space in its general hospitals, which are equipped for most advanced types of medical and surgical attention. From its general hospitals it has started to move men who can get around and who do not need constant medical and surgical attention. Still unanswered is the question of whether the Army and Navy will continue to operate all the hospitals built for the services when the war is over. Alternative would be to turn them over to the Veterans Administration. Also undetermined is which hospitals will be turned back to civilian uses and which will be kept by the government as the number of hospitalized men decreases. The Army is expected to reveal soon an extensive program of convalescent hospitals for wounded veterans. Its main purpose will be to provide accommodation for thousands of long time convalescents able to walk and exercise.

Venereal Disease Control Advocated

Favorable editorial reaction to the conference on venereal disease concluded recently in St. Louis was expressed in the press of the Capital, with the Washington *Post* making a specific proposal that "the problem of controlling the disease seems to lie in finding a way to control it among women." Admitting the difficulties involved, it adds "But since few of the women who are now spreading the infection are professional prostitutes, the thing is much easier proposed than accomplished."

U. S. Backs Liberian Health Plan

The United States Public Health Service announces that an all Negro United States mission, including physicians, engineers, entomologists and nurses, soon will launch a five year health and sanitation program in Liberia, West Africa. The mission was organized at President Roosevelt's direction on request of the Liberian government and will be headed by Dr. John Baldwin West, senior surgeon, U. S. P. H. S.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Two Deaths from Mussel Poisoning.—The quarantine established May 1 of all mussels from the ocean shore of California, including the Bay of San Francisco, has been extended until further notice as the result of 9 cases of mussel poisoning with two deaths in San Mateo County.

University News.—Francis J. W. Roughton, Ph.D., fellow of Trinity College, Cambridge, and fellow of the Royal Society of London, who has been working in the United States on aero medical problems, recently delivered a lecture in Wheeler Hall, University of California, Berkeley, on "Some Recent Work on Carbon Monoxide as a Poison and a Physiological Tool."

School Health Educator Named.—The state department of public health announced the appointment as school health educator of Miss Bernice Moss, recently lecturer in public health education in the University of California School of Public Health. The state department of education is cooperating with the state department of public health in promotion of the school health education program. Miss Moss, who has a master's degree in health education, will be available for consultant service in the state public schools.

Personal. — Stanley B. Freeborn, Ph.D., United States Public Health Service, who, after Pearl Harbor, organized and administered the program of the public health service for malaria control in war areas, has returned to his position as professor of entomology and assistant dean of the University of California College of Agriculture, Berkeley.——Dr. Eberle Kost Shelton, Los Angeles, was recently given the honorary degree of doctor of science by the University of Colorado School of Medicine, Denver, where he graduated in 1911.

COLORADO

Personal. — Dr. Alfred Lee Briskman, assistant medical director of the Union Printers Home and Tuberculosis Sanatorium, Colorado Springs, has been appointed medical director at the Jewish Consumptives' Relief Society sanatorium in Denver. Dr. James H. Riffey will succeed Dr. Briskman at the printers' home.——Dr. William H. Crisp, Denver, was recently presented with a watch by the *American Journal of Ophthalmology* in appreciation of his long service to the journal and for outstanding contributions to ophthalmology.

Division of Industrial Hygiene Revived.—A. T. Rossano Jr., M.S., has been lent by the U. S. Public Health Service to the Colorado State Board of Health to serve as director of and to reactivate the division of industrial hygiene. The division became inactive more than two years ago, when the entire staff was called into the armed services. The staff of the division will consist of an industrial hygiene engineer, an industrial hygiene chemist and the part time services of an industrial physcian and an industrial nursing consultant. A completely equipped industrial hygiene laboratory will be maintained for precise analyses of atmospheric samples, materials and biologic fluids. Special field instruments for the rapid evaluation of occupational hazards will be available.

FLORIDA

Physician Fined $10,000 for Narcotic Violation.—On November 7 the Tampa *Tribune* reported that Dr. Benjamin L. White, St. Petersburg, had, the previous day, been fined $10,000 and given a suspended sentence of two years and a day in a federal penitentiary after pleading nolo contendere to 26 charges of illegally selling narcotics. In addition to the fine and suspended sentence, the physician was placed on probation for five years, three of them under the supervision of a federal probation officer. Specific provisions of the probation were that he pay the fine within thirty days, surrender his narcotic license and all narcotics, and refrain from prescribing or dispensing narcotics in any form during his five years' probation. The *Tribune* reported that Dr. White admitted his guilt to a similar indictment of 28 charges ten years ago in Orlando but owing to his past record was allowed to make a compromise settlement with the government of $1,500. The case was heard by District Judge William J. Barker, Southern District of Florida, and the $10,000 fine was said to be the largest criminal fine ever made in that federal court.

GEORGIA

New Quarantine Hospital.—October 19 was to be the opening date for the new $40,000 quarantine hospital in Atlanta. The new unit is located in a remodeled building at the city prison farm and is under the supervision of the city department of health. Dr. James F. Hackney is the city health director.

Personal.—David F. Marsh, Ph.D., assistant professor of pharmacology, University of Georgia School of Medicine, Augusta, has been appointed associate professor of pharmacology and head of the department at the West Virginia University School of Medicine, Morgantown, effective December 31. Raymond P. Ahlquist, Ph.D., has been appointed assistant professor of pharmacology at Georgia to succeed Benedict E. Abreu, Ph.D.

Dr. Paullin Honored. — On November 21 the Atlanta Chamber of Commerce awarded its annual Certificate of Distinguished Achievement to Dr. James E. Paullin, former President of the American Medical Association. More than 200 persons were present for the ceremony, which included a dinner in the Onsley Hotel. The citation accompanying the award read:

> To James Edgar Paullin in recognition of service, practical in nature, to the welfare of the people of this state and nation. For more than thirty-seven years Dr. Paullin has worked faithfully to improve standards in hospitals, in the practice of medicine and in medical education. Testimony to the effectiveness of his work and its value to the medical profession has already been given by the distinguished medical societies of the country. It is fitting that his friends and neighbors show, by this certificate, that they understand and appreciate the value of his services to his own community.

Expansive Postwar Hospital Program.—On recommendation by its health panel, the state agricultural and industrial development board of Georgia approved, November 9, a large expansion of facilities for medical care and hospitalization in Georgia as a postwar project. According to the New York *Times*, the program contemplates the expenditure of $22,545,000 local funds and $5,275,000 state funds for the purchase or construction of hospitals and the provision of $3,535,000 local funds and $7,925,000 state funds for their operation. It also proposes buying 5,660 general hospital beds in fifty-three counties. The panel reported that eighty-six counties had no general hospital beds and only six counties had more than five beds in 1,000 population. It added that two counties did not have a resident physician and seventy-six had only one physician each in 3,000 population. The agricultural and industrial development board was created recently by the general assembly to coordinate existing agencies. Seven panels constitute the board, covering agriculture, education, government, health, industry, public works and trade, commerce and business. Members of the health panel include Dr. Thomas F. Abercrombie, Atlanta, chairman, and Dr. Rufus F. Payne, Atlanta, director. Headquarters of the board are located on the campus of the University of Georgia, Athens.

ILLINOIS

Ninety Years of Age.—Dr. James M. Mitchell, Oblong, celebrated his ninetieth birthday October 19 as the guest of the Crawford County Medical Society. Dr. Mitchell graduated at the Hospital College of Medicine, Louisville, Ky., in 1901.

Citizens Vote to Establish Health Departments and Tuberculosis Control. — New health departments will be created in Adams and Du Page counties through the vote of the people in the recent election. In Adams County the vote passed by a three to one majority and in Du Page County by a three to two majority. This is said to be the first time that people of any county in the state have by popular vote established a county health department and levied a tax to support it. These two counties were the first to submit the provision to a vote under the new law popularly known as the Searcy-Clabaugh law.——In Clinton and Edwards counties citizens voted favorably for the first time for a tax levy to provide for the care and treatment of their tuberculous citizens as provided by the Glackin and Excess Tax laws. Tazewell County, already operating under the provisions of the Glackin law, voted favorably on the levy of a special tuberculosis tax in excess of the ordinary tax limits. Nine other counties also voted favorably on the proposition, some to legalize and some to continue the excess

tax levy for the control of tuberculosis. These counties include Bureau, Champaign, Clay, Hardin, Jasper, McDonough, Rock Island, Sangamon and Shelby. Of the 102 counties in Illinois, 83 have now voted favorably on a tax levy for tuberculosis control. The 19 remaining counties that have not voted a tax, and very few of which have tuberculosis control programs of consequence, include Brown, Calhoun, Edgar, Hancock, Jersey, Jo Daviess, Johnson, Lawrence, Marshall, Massac, Monroe, Perry, Pope, Pulaski, Putnam, Union, Wabash, Warren and Williamson.

Chicago

The Fenger Lecture.—Col. Esmond R. Long, M. C., will deliver the ninth Christian Fenger Lecture of the Institute of Medicine of Chicago and the Chicago Pathological Society at the Palmer House, January 8. His Subject will be "Tuberculosis as a Military Problem."

Symposium on Obstetrics.—The Chicago Medical Society will devote its December 13 meeting to a symposium on obstetrics. The following will participate:

Dr. Theodore J. Morris, Diagnosis and Treatment of Puerperal Infection.
Dr. William J. Dieckmann, Early Signs and Treatment of Toxemia of Pregnancy.
Dr. Janet E. Towne, Prolonged Labor.
Dr. Frederick H. Falls, Proper Use of Cesarean Section.

MASSACHUSETTS

District Meeting.—The Suffolk District Medical Society was addressed in Boston, November 18, by Governor Leverett Saltonstall on "Medical Social Security" and Dr. Roger I. Lee, Boston, President-Elect of the American Medical Association, "Health Insurance?"

Seventy-Five Years of Public Health.—The Massachusetts Department of Public Health is this year completing seventy-five years of service. According to Dr. Vlado A. Getting, Boston, state health commissioner, in the *Norfolk Medical News*, the Massachusetts board was the first in America.

Licenses Revoked.—At a meeting of the state board of registration in medicine, October 18, the license to practice medicine of Dr. Robert E. Conlin, Woburn, was revoked because of gross misconduct in the practice of his profession as shown by his conviction in court and treatment of a patient. The license to practice was also revoked of Dr. Morris J. Kupper, Roxbury, because of gross misconduct in the practice of his profession as shown by collusion.

Riggs Foundation Observes Anniversary.—The Austen Riggs Foundation, Stockbridge, commemorated its twenty-fifth anniversary with a meeting at the New York Academy of Medicine, November 22. The foundation, directed by a board of trustees, a medical advisory board and the Austen Riggs Associates continues in the village of Stockbridge the medical practice of the late Dr. Austen Fox Riggs, which was restricted to the care and treatment of mild nervous or functional disorders. Among the speakers were Dr. Lawrence S. Kubie, New York, who discussed the problem of brief psychotherapy and the training of therapists, Brigadier John R. Rees, British army, and Major General George B. Chisholm, Canadian army.

NEW YORK

Graduate Lectures.—Richard C. Arnold, Surgeon, U. S. Public Health Service, gave a graduate lecture on "Penicillin Therapy" before the staff of Veterans Memorial Hospital, Ellenville, December 5, and Dr. Julian Rose, Brooklyn, addressed the Saranac Lake Medical Society, December 6, on "Diseases of the Biliary Tract." Dr. William F. Lipp, Buffalo, will address the Jefferson County Medical Society in Watertown, December 14, on "Treatment of Jaundice." These lectures are sponsored cooperatively by the state medical society and the state department of health.

Personal.—Dr. Gilbert Dalldorf, director of the Grasslands Hospital laboratory, Valhalla, has been appointed director of the new Westchester Health Laboratory, which is to be set up at Grasslands.——Dr. Eugene Kisch, New York, associate in orthopedic surgery, Hospital for Joint Diseases, Far Rockaway, left for Brazil in October to lecture on bone and joint tuberculosis and to attend conferences in Rio de Janeiro, São Paulo and Bello Horizonte as the guest of the Brazilian Society for Tuberculosis.——Dr. Moses A. Stivers, Middletown, has been appointed to the recently created position of medical consultant to the department of public welfare, it is reported.——Dr. John S. Ware has been appointed chairman of the health committee of the Staten Island Council of Social Agencies.

New York City

Harvey Lecture.—Dr. Jean R. Oliver, professor of pathology, Long Island College of Medicine, Brooklyn, will deliver the third Harvey Society Lecture of the current series at the New York Academy of Medicine, December 21. His subject will be "New Directions in Renal Morphology: A Method, Its Results and Its Future."

Lectures to the Public.—On November 9 the New York Academy of Medicine opened its tenth series of lectures to the public with a talk by Dr. Iago Galdston on "Psychiatry in the History of Medicine." The opening address was designated the Linsly R. Williams Memorial Lecture. Other lectures in the series, which this year has been devoted to "Psychiatry in Medicine," include:

Dr. James H. Wall, White Plains, N. Y., Development of Modern Psychiatry, November 20.
Dr. G. Canby Robinson, Washington, D. C., The Patient as a Person, December 19.
Dr. Franz G. Alexander, Chicago, Recent Trends in Psychiatric Thought and Future Outlook, December 28.
Col. William C. Menninger, M. C., War and Psychiatry, January 11.
Dr. Edward Weiss, Philadelphia, Psychotherapy in Everyday Medicine (George R. Siedenburg Memorial Lecture), January 25.

Presentation of Nobel Awards.—On December 10 six of eight winners of the 1943-1944 Nobel Prizes in science and literature will receive awards amounting to $120,000 at a luncheon in the Waldorf-Astoria Hotel. The occasion, which is being sponsored by the American-Scandinavian Foundation, 116 East 64th Street, will mark the first time that the Nobel Prizes ever have been presented in the United States. The presentations will be made on behalf of King Gustav V by Wollmar F. Boström, minister from Sweden. Recipients of the awards will be, among others, Henrik Dam, Rochester, N. Y., and Edward A. Doisy, Ph.D., St. Louis, for their work on vitamin K; Drs. Joseph Erlanger, St. Louis, and Herbert S. Gasser, director of the Rockefeller Institute for Medical Research, for their work on nerves, and Isidor I. Rabi, Ph.D., and Otto Stern, Ph.D., Pittsburgh, for the results of their study of the structure of the atom.

Medical Societies Coordinating Council Considers Reorganization.—A plan has been presented to reorganize the coordinating council of the five county medical societies of greater New York in order that official representatives of each group may form an authoritative body to represent the organized medical profession in the city. According to the *Journal* of the Medical Society of the County of New York, each county medical society is now completely autonomous, speaking for the profession only within its own boundaries. It may or may not take into consideration the interests of the four other county medical societies in the city. In matters of identical interest each society may take a stand, either in agreement or in conflict with the interests of the other county medical societies or the action taken by them. While the coordinating council of the five county medical societies has been of service during the ten years of its existence, the council has, however, lacked the authority and power to do more than advise or suggest. Under the recommendation to reorganize the council, it is proposed that each county medical society retain its autonomy within the state society but that it alter or amend its constitution and by-laws to grant certain definite powers to the coordinating council of the five county medical societies, electing to it annually three representatives, which under the new setup would be enabled to speak with authority on matters involving all the county medical societies generally but excluding matters of purely intracounty interest or import. Each county medical society would retain all powers not granted to the coordinating council. The proposal carries certain stipulations as to the method of action by the council in the handling and commitment of its powers. The functions of the council would be supported by contributions from each of the five county societies on a per capita basis according to the membership of each society and would have a headquarters office with a director and other clerical help.

PENNSYLVANIA

Society News.—Dr. Louis H. Clerf, Philadelphia, addressed the Reading Eye, Ear, Nose and Throat Society, November 15, on "Cough Considered from an Otolaryngologic Viewpoint."——The Pennsylvania State Association for Health, Physical Education and Recreation held its annual conference at the Schenley Hotel, Pittsburgh, December 8-9. The address of the association is 231 Administration Building, Forbes Street at Bellefield Avenue, Pittsburgh 13.

Howard Petry Appointed Director of Mental Health.—Dr. Howard K. Petry, medical superintendent of the Harrisburg State Hospital, has been appointed director of the bureau of mental health of the Pennsylvania Department of

Welfare. He succeeds Dr. William C. Sandy, who retired from the position July 1 (THE JOURNAL, August 12, p. 1050). Dr. Petry, who has been chairman of the committee on mental hygiene of the Medical Society of the State of Pennsylvania for many years and who recently was appointed by the governor as chairman of a committee to make a survey of conditions in the state's mental hospitals, will continue to serve as superintendent of the Harrisburg State Hospital.

Philadelphia

Personal.—Dr. Harvey Bartle has retired as medical director of the Pennsylvania Railroad after forty-one years of service. Dr. John A. White, medical examiner for the company in Washington, D. C., for a number of years, has been named to succeed Dr. Bartle as chief medical examiner.

Schireson's Trial Scheduled for January.—Hearing on the injunction sought by Dr. Henry Junius Schireson to prevent the state from revoking his medical license has been scheduled for the January term of the Dauphin County Court, Harrisburg, the Philadelphia *Record* reported November 22. It was stated that Schireson was ordered by the state board of medical education and licensure last June to appear on July 10 and show cause why his license should not be revoked on the ground that it was obtained through fraud (THE JOURNAL, May 27, p. 297). Subsequent investigation by the state licensing board, with the assistance of the attorney general's office, disclosed that when Schireson applied for his license to practice in Pennsylvania in 1910 he pretended to medical qualifications he did not have. Schireson obtained a temporary injunction restraining the state from holding a hearing on the "show cause" order (THE JOURNAL, September 9, p. 116), contending that the state had no authority to revoke a license for fraud, it was stated. This action was taken in July and since then time has been spent in an effort to find a time convenient for the court, for the state and for Schireson when arguments could be heard on the issue of whether the injunction should be vacated or made permanent.

TEXAS

State University to Remain at Galveston.—The board of regents of the University of Texas at its recent annual session voted six to one in repudiation of a recent recommendation that the medical school of the university be moved from Galveston to Austin. The board also accepted an offer of the Sealy and Smith Foundation, Galveston, to give $2,000,000 for construction of a new general hospital to provide more clinical material for the medical school.

Science Meeting.—The Texas Academy of Science met in Galveston, November 9-11, under the auspices of the University of Texas Medical Branch. Features of the session included a symposium on age changes in various tissues, symposium on health conditions in the coastal area of Texas, a discussion on the establishment of a marine biologic laboratory, several sessions on the conservation of natural and human resources and a symposium on the biology of the cancer cell.

Plans Approved for New Medical Building at Baylor.—At a meeting of the board of trustees of Baylor University, November 13, tentative building plans were approved for a new college of medicine building to be erected on the 20 acre site in the medical center. The proposed four story building will cost $1,000,000. It will include an auditorium in the center wing and will house all the preclinical and administrative departments as well as offices for the members of the clinical departments. The $1,000,000 for the new building and the 20 acre site are gifts to the college by the M. D. Anderson Foundation, which has also provided $1,000,000 for research to be used in the next ten years. In addition, the college of medicine received $500,000 for the same ten year period as a gift from the citizens and business firms of the city of Houston.

Personal.—Dr. Benjamin F. Hambleton, professor of physiology and pharmacology, Baylor University College of Medicine, Houston, was recently awarded the honorary doctor of science degree "in recognition of his long service in medical education and research." Dr. Hambleton has been with Baylor since 1920. Previously he was professor of physiology and pharmacology at Vanderbilt University School of Medicine, Nashville, Tenn., where he also served as acting dean and secretary of the medical school during World War I.——Dr. William W. Looney, for many years professor of anatomy, Baylor University College of Medicine, Houston, and recently professor and chairman of the department of anatomy, Southwestern Medical College, Dallas, has resigned to enter private practice in Greenville.——Dr. Edward F. Yeager, Mineral Wells, was recently appointed medical director of the Baker Hotel, a newly inaugurated service for guests who register to take the baths and water.

VERMONT

Personal.—Dr. James C. O'Neil on July 15 resigned as medical superintendent and treasurer of the Vermont State Hospital for the Insane, Waterbury.

State Medical Election.—Dr. Leon E. Sample, St. Albans, was chosen president-elect of the Vermont State Medical Society in October and Dr. Frank J. Hurley, Bennington, was installed as president. Other officers include Drs. Paul C. T. Bacon, Springfield, vice president; David Marvin, Essex Junction, treasurer, and Benjamin F. Cook, Rutland, secretary.

VIRGINIA

Vaughan Memorial Clinic.—The Vaughan Memorial Clinic is now being developed in Richmond as a memorial to the late Dr. Warren Taylor Vaughan. The clinic may be considered at the present time as an outgrowth of the Vaughan-Graham Clinic, which was established jointly by Dr. Vaughan and Dr. William Randolph Graham. Dr. John Warrick Thomas recently became associated with the clinic.

WASHINGTON

Medical Society Dedicates Bulletin to Doctors Hospital.—The King County Medical Society designated its November 20 Bulletin the Doctors Hospital issue in honor of the recent completion of the hospital. The bulletin contains historical material and illustrations of the new unit as well as a history of the King County Medical Service Corporation. Doctors Hospital, according to the bulletin, represents a "milepost in the life journey" of the King County Medical Society. The approximate cost of one million dollars included an allocation of $665,000 by the FWA. The remainder was provided by the medical service corporation (THE JOURNAL, Dec. 18, 1943, p. 1059 and Nov. 25, 1944, p. 847).

WEST VIRGINIA

Changes in Health Officers.—Drs. Allen E. LeHew, Lewisburg, and James R. Richardson, Union, have been appointed part time health officers for Greenbrier and Monroe counties, respectively, succeeding Dr. Herbert Duncan, former district health officer, who is now in Nashville, Tenn.——Dr. Garnett P. Morison, Charles Town, has been appointed as part time health officer of Berkeley County, to succeed Dr. Henry R. Dupuy, Martinsburg.

GENERAL

Social Hygiene Day.—February 7 has been announced by the American Social Hygiene Association as National Social Hygiene Day. Special educational observances will be held throughout the country.

Federation for Clinical Research.—Investigators wishing to present papers before the Southern section of the American Federation for Clinical Research in Dallas some time in January are instructed to send abstracts of not more than 200 words to the chairman, Dr. Alfred W. Harris, 1719 Pacific Avenue, Dallas 1, by January 1. The Southern section is planning a two day meeting, the exact dates for which have not yet been announced.

Injuries in Coal Mines.—Final figures on injuries in coal mines in the United States in 1942, the first full calendar year of American participation in the war, reveal that accident frequency rates that year were the lowest since 1930 and that production of coal per man-hour of work was the highest in the nation's history, according to the Bureau of Mines, Department of the Interior. Compilations by the accident analysis division show that 530,861 men were employed in anthracite and bituminous mines in 1942, a decline of 15,831 from 1941. These employees produced a record total of 640,000,000 tons, of which 582,000,000 came from the bituminous fields and 58,000,000 from the anthracite region of Pennsylvania. To produce this quantity of coal, 1,471 men lost their lives and 69,564 men suffered nonfatal injuries that disabled them for more than the remainder of the day on which the accident occurred, the bureau reported in a publication analyzing accidents for 1942. Assuming a uniform payment of $5,000 for each fatality and $100 for each nonfatal accident, the bureau estimated that injuries cost the nation about $14,311,400 in compensation payments. Chief causes of accidents in both bituminous and anthracite mines were falls of roof, first, and haulage (transportation), second. Proving that fatalities can be prevented in coal mines, 6,201 of the 6,940 bituminous mines listed in the bureau's compilation worked through 1942 without a death.

Association for Research in Nervous and Mental Disease.—The twenty-fifth annual meeting of the Association for Research in Nervous and Mental Disease will be held at the Waldorf-Astoria Hotel, New York, December 15-16, under the presidency of Col. Franklin G. Ebaugh, M. C. Among the speakers will be:

Dr. John C. Whitehorn, Baltimore, Changing Concepts of Psychoneurosis in Relation to Military Psychiatry.
Lieut. Col. Malcolm J. Farrell and Major Norman Q. Brill, M. C., Neurotic Reactions in Psychopaths.
Lieut. Col. Roy R. Grinker, M. C., A Dynamic Study of War Neuroses in Fliers Returned to the United States.
Drs. Edward A. Strecker and Kenneth E. Appel, Philadelphia, Psychiatric Contrasts in the Two World Wars.
Brigadier John R. Rees, British army, Development of Psychiatry in the British Army.
Brig. Gen. Eugen I. G. Reinartz, Research Aspects at the AAF School of Aviation Medicine in Nervous and Mental Diseases.
Major Gen. George B. Chisholm, Canadian army, Psychological Problems of Demobilization.
Col. William C. Menninger, M. C., Problem of the Discharged Neuropsychiatric Patient.
Capt. Lewis L. Robbins, M. C., Mental Hygiene Unit, Army Air Forces.
Major Fred F. Senerchia Jr., M. C., An Experimental Unit for the Retraining of Psychoneurotic Soldiers.
Lieut. Col. Guy C. Randall and Major Harry C. Blair, M. C., and Dr. Jack R. Ewalt, Galveston, Psychiatric Reactions of Patients with Amputations.
Capt. David G. Wright, M. C., Anxiety Related to Aerial Combat.
Major Ivan C. Berlien and Lieut. Col. Frederick R. Hanson, M. C., Psychiatry in the Combat Division.
Lieut. Col. Ralph T. Collins, M. C., Neuropsychiatry with an Overseas Evacuation Hospital.
Lieut. Comdr. Herbert I. Harris (MC), Importance of the Emotional Outlet in Psychotherapy.
Lieut. Comdr. Howard P. Rome (MC), Psychopathology and Group Therapy.
Comdr. George N. Raines, Lieut. Comdr. Leslie B. Hohman and Lieut. Comdr. Lawrence C. Kolb (MC), Methods of Recovery in Combat Fatigue and the Influence of Therapy.
Lieut. Manuel M. Pearson and Lieut. Comdr. Robert A. Cohen (MC), Psychotherapy in a Naval Convalescent Hospital.
Drs. Lawrence S. Kubie and Sydney G. Margolin, New York, Therapeutic Role of Drugs in the Processes of Repression, Dissociation and Synthesis.
Capt. Ephraim Roseman, M. C., Electroencephalography and Head Injury.
Major George M. Haas, M. C., Head Injuries in Aircraft Accidents.
Major Frank H. Mayfield and Capt. John W. Devine Jr., M. C., Causalgia.
Drs. Lewis J. Pollock, James G. Golseth and Alex J. Arieff, Chicago, Electrodiagnosis of Peripheral Nerve Lesions.
Major Herman B. Snow, M. C., Psychiatric Procedure at the Rehabilitation Center, Second Service Command.
Lieut. Col. Walter E. Barton, M. C., Convalescent Reconditioning Program for Neuropsychiatric Casualties in the U. S. Army.
Col. John H. Baird, M. C., Neuropsychiatric Problems of the Veterans Administration.
Dean A. Clark, senior surgeon, U. S. Public Health Service Reserve, and Victor H. Vogel, surgeon, U. S. Public Health Service, Mental Illness and the Expanded Federal-State Vocational Rehabilitation Program.
Dr. Leonard E. Himler, Ann Arbor, Mich., Psychiatric Rehabilitation in Industry.

Additional Grants for Physical Medicine.—A new group of seven grants aggregating $185,000 has been announced by the Baruch Committee on Physical Medicine. The new grants include $50,000 to the Massachusetts Institute of Technology, Cambridge, Mass; $40,000 to the University of Minnesota Medical School, Minneapolis; $30,000 to Harvard Medical School, Boston; $30,000 to the University of Southern California School of Medicine, Los Angeles; $15,000 to the State University of Iowa College of Medicine, Iowa City; $15,000 to the University of Illinois College of Medicine, Chicago, and $5,000 to Marquette University School of Medicine, Milwaukee. The grants to the Massachusetts Institute of Technology and the University of Minnesota are in addition to the gift of $1,100,000 made by Mr. Baruch in April, at which time grants were made to Columbia University College of Physicians and Surgeons, New York University College of Medicine, the Medical College of Virginia, Richmond, and for minor research and fellowship programs for the advancement of physical medicine. The present gift to the Massachusetts Institute of Technology is in support of a five year program of training and research in electronics, instrumentation and physics in relation to medicine, to be carried on under the auspices of the department of biology and biologic engineering. It was the conviction of the scientific advisory committee of the Baruch Committee on Physical Medicine that Baruch Fellows and other physicians should have more than a superficial knowledge of the physics and technology underlying the physical methods and instrumentation used in this field, and it was suggested that training in this aspect might effectively be centered at the Massachusetts Institute of Technology. The program will be under the general supervision of Francis O. Schmitt, Ph.D., head of the department of biology and biologic engineering and under immediate supervision of Kurt S. Lion, D.Eng., assistant professor of applied biophysics, who is an expert in physical instrumentation. The grant of $40,000 to the University of Minnesota is to support the development of a three year teaching and fellowship program in physical medicine. The primary objective of the program is to be the furtherance of fundamental training of research workers and teachers. The program has as its basis the development of scientists in the field of physical medicine. As an auxiliary to this basic training facilities will be developed for the training of clinicians and technicians. The other grants have been allocated from the fund of $200,000 given by Mr. Baruch in April. The sum of $30,000 was granted to Harvard Medical School for establishment of a three year program to provide fellowship or residencies to be used for the benefit of qualified physicians who are selected to be trained in this field. This sum will be administered by a strong standing committee on physical medicine recently appointed by Dr. C. Sidney Burwell, dean of the Harvard Medical School, composed of Drs. James B. Ayer, Derek E. Denny-Brown, William T. Green, James H. Means, Arthur L. Watkins and Eugene M. Landis, chairman. Appointments to the fellowships, which generally carry stipends of $2,500, will be made annually but may be renewed to provide up to three years of specialized study and research. Emphasis will be placed on training a few men in basic research and clinical investigation. Unusual opportunities for clinical experience and research in the psychologic and psychiatric aspects of physical medicine will be available at Harvard. The first year will be wholly or in part devoted to basic research related to physical medicine in one of the preclinical sciences such as physiology, anatomy or biophysics. The second year will be spent in clinical training in physical medicine at the Massachusetts General Hospital and other hospitals affiliated with the Harvard Medical School. In the third year, fellows will be assistants in physical medicine with clinical responsibilities. For candidates with extensive previous training, one year clinical fellowships will also be granted. Applicants must have an M.D. degree from an approved medical school and a minimum of one year of internship in an approved hospital. Applications may be obtained from the Dean, Harvard Medical School, 25 Shattuck Street, Boston 15. The sum of $30,000 is granted to the University of Southern California to inaugurate a program of teaching and research in physical medicine in its medical school. The sum of $15,000 is granted to the University of Illinois to inaugurate a teaching program in physical medicine at its medical school. The sum of $15,000 is granted to the University of Iowa to assist in a joint research and teaching program concerning the effectiveness of different methods of applying heat to the deep tissues of the human body. Finally, the sum of $5,000 is granted to Marquette University for continuance of research in the physiology and pathology of nerves and muscles as related to physical medicine. In discussing these grants Dr. Frank H. Krusen, director of the Baruch Committee, pointed out that Mr. Baruch had been particularly interested in the important field of electronics as applied to medicine and he said that the center at the Massachusetts Institute of Technology gave promise of revolutionizing the application of electronics in the diagnosis and treatment of the sick. Dr. Krusen announced that the administrative board of the Baruch Committee does not contemplate the recommendation of any further large grants for the establishment of additional departments of physical medicine in our medical schools. Main attention will now be directed to the adequate development of the centers already established and to providing advice in the organization of proper teaching of physical medicine in medical schools, and, through the committee on war and postwar physical rehabilitation and reconditioning, an attempt would be made to promote proper development of physical medicine in the rehabilitation and reconditioning of both military and civilian casualties of war.

CORRECTION

Digitalis Poisoning.—In the article by Herrmann et al. which appeared in the November 18 issue of THE JOURNAL, table 2 is a duplication of table 1, table 3 should be table 2, and the following table was omitted:

TABLE 3.—*Types of Heart Disease Affected by Digitalis Poisoning*

Hypertensive	Hyp. A. S.	Hyp. Syph.	A. S.	Syph.
21	8	4	5	3
Rheumatic		Congenital	No Heart Disease	
1		1	1	

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 4, 1944.

Social Insurance and Family Allowances

The social insurance scheme of the government, which affects the life of every person from the cradle to the grave, has been unanimously approved in the House of Commons. Mr. Butler, minister of education, moved that the House "welcome the intention to establish an enlarged and unified system of social insurance and a system of family allowances." He said that the various schemes for social betterment expressed the universal desire for a more closely knit society, in which all shared together both the risks and the opportunities. They seemed to concentrate more on the younger generation and on children and also to insist that in the interest of the country and the workers the government must push ahead with the policy of full employment. Every child should be guaranteed the best possible basis of physical health, but it was difficult to calculate or guarantee the nature of the benefits which the child received. The system of family allowances, he said, was intended to help the general economy of the family and was not intended to be based on any question of subsistence. The family was expected to maintain the first child, he explained, because the family should continue to have responsibilities of its own, especially in regard to the first child, and because its inclusion in the benefits would more than double the cost of the scheme. The real argument for family allowances, he said, was that they helped a family to stand the strain where it was felt most. He had been asked whether or not family allowances would raise the birth rate. That was not the government's sole reason for introducing them, he answered, but it hoped that an increase would result. The plan would give greater confidence to our families.

Regarding assistance in kind, the provision of meals and milk had already been established on a large scale, but the government's view was that this policy must now be carried to its logical conclusion. In spite of war difficulties, the number of children taking their midday meal at school had risen from 300,000 to 1,600,000. But there was a long way to go before all children got their meals at school, the minister stated. The government had decided that when the immediate urgency for house repairing in London was finished, school meals should be given an equal priority with the other most urgent needs of the country. School milk could be made free at the same time cash allowances were introduced. School meals on this scale were something new in our social system, he pointed out, giving all children a "fair start" physically.

Children under 5 years old had been regarded as a gap in the government's policy, Mr. Butler stated. The national milk scheme and the provision of welfare foods—orange juice, cod liver oil, and so forth—which was an important part of the wartime plan, would be continued for a while. There was no country in the world, he said, which had been able to introduce such a vast program of social reform as we had done and at the same time defeat one of the greatest tyrants in history.

Few voices of criticism have been heard against this vast system of social insurance and family allowances. Even the conservative *Times* gives the scheme unqualified support in its editorials. Endorsing the government White Paper, it declares that the scheme is a concrete expression of the solidarity and unity which in war have been the nation's bulwarks against aggression and in peace will be its guaranty of success in the fight against individual want and misfortune. The *Times* also endorses the government's decision not to allow any group in the community to claim exception from insurance. Those who by reason of their own superior security are not willing to share the risks of all are described as claiming the right, which cannot be admitted, to "make a separate peace with want."

Professor Ernest W. Hey Groves

The death of Professor Hey Groves, at the age of 72 years, has removed a prominent figure in British surgery. He began his medical life as a general practitioner but soon became interested in surgery. He obtained the Fellowship of the Royal College of Surgeons and was appointed to the surgical staff of the Bristol General Hospital. He also became senior demonstrator in anatomy at Bristol University. A mechanical turn of mind led him to specialize in orthopedics, and he invented numerous orthopedic splints and devices. Before the introduction of the Smith-Petersen nail he worked at improving the operative treatment of fractures of the neck of the femur by fashioning pins of beef bone and of the horn of the stag and the rhinoceros. In 1913 he advocated the fixation of fractures by steel pins passed through the bone and attached to outside supports. This required only the use of a drill instead of the more complicated plating then in general use. His work in the last great war increased his reputation, and in 1915 he produced a primer on "Gunshot Injuries of Bones." Other successful works from his pen were his "Synopsis of Surgery" (1908), "Modern Methods of Treating Fractures" and "Surgical Operations." He was president of the British Orthopedic Association in 1928-1929 and of the Association of Surgeons of Great Britain and Ireland in 1929-1930. He edited the *British Journal of Surgery* from its inception in 1913 throughout almost its whole career of preeminence in surgical literature, until advancing years compelled him to resign in 1941. His guidance played a large part in its success.

Sheltered Employment for the Disabled

Sir Godfrey Ince, director general of man power, has stated in a speech at Manchester that a company controlled and financed by the Ministry of Labor is to be formed to provide sheltered employment for severely disabled persons who cannot hold their own in competitive industry. It was unlikely that the whole employment of the disabled could be dealt with by voluntary organizations, the director stated. The special company and any voluntary organization receiving assistance from the Ministry of Labor must be required to apply its profits, if any, to promoting these objects, it was explained, and will be prohibited from paying any dividend to its members.

The Editorship of the Lancet

The proprietors of the *Lancet* have announced with much regret the retirement of Dr. Egbert Morland from the editorial chair. He joined the staff of the *Lancet* in 1915 and has been editor since 1937. He has well sustained the reputation of the journal as both a scientific and a political organ of the profession. The Royal College of Physicians and the Royal College of Surgeons have shown their appreciation of his work by admitting him to their fellowship. He is succeeded by Dr. T. F. Fox, who has been for some years assistant editor. He will be assisted by Dr. E. Clayton-Jones.

Oil Cargo Under Red Cross Flag

After the British submarine *Unruly* had engaged an enemy ship with gunfire, which caused the crew to abandon ship, it is reported, the submarine drew nearer and it was then seen that the enemy vessel was flying a Red Cross flag and had red crosses on her bow. The commanding officer of the submarine, Lieut. J. P. Fyfe, decided to examine her before sinking her. He found that she was not so innocent as she looked. Her cargo consisted of oil in drums, and the Nazi ensign was found under the captain's pillow. As she was clearly a supply ship,

she was blown up. Such abuse of the Red Cross was perhaps to be expected; many times during the war the Germans have shown no respect for either the Red Cross or the Geneva Convention, to which they are signatories, by attacking and sinking hospital ships plainly marked as such and by killing medical staff, nurses and patients.

Whiter Bread

One of the measures adopted by the government to insure a sufficient supply of food for all was to enforce an 85 per cent extraction of the national flour from wheat. A new order has been made decreasing the rate of extraction to 82.5 per cent. The object is stated to be to improve the national bread. The new flour will produce a whiter and better quality loaf, with no appreciable loss of nutritional value.

BUENOS AIRES

(From Our Regular Correspondent)

Oct. 11, 1944.

Medical Care and Social Insurance

Dr. José Arce of Buenos Aires recently lectured before an audience at the Centro de Estudiantes de Medicina on medical care and social insurance. More than 60 per cent of the Argentine population have an income of less than $1,200 a year, he said. Families with such incomes have a right to free medical care by the state, he thought. He also recommended a large department for medical assistance, with branches in several provinces. The members of the department would supervise the work of family physicians, hospitals and centers of social medical care. A large number of additional hospital beds are necessary, according to Dr. Arce, 84,000 beds to be given free of any charge to people in need of social aid, 42,000 beds to be given to patients belonging to families with incomes of from $1,250 to $3,000 and 14,000 for patients who can pay a reasonable amount. It is advisable to establish medical councils and hospital councils to supervise the medical and hospital work in the country, he added.

Thyroid and Metathyroid Diabetes

Dr. Bernardo A. Houssay of Buenos Aires, president of the Argentine Society of Biology, and Dr. Oscar Orías, also of Buenos Aires, recently lectured before the society. According to Houssay, prolonged administration of thyroid does not cause diabetes in normal dogs, whereas it does cause the disease in dogs with normal glycemia and a pancreas experimentally reduced to 2.5 or 2.3 Gm. The animals are more susceptible to the disease when they are treated by administration of thyroid or preparations of the anterior lobe of the hypophysis before the administration of thyroid. The disease may be of the thyroid type, which lasts only during administration of thyroid extract, or of the metathyroid type, which persists even after discontinuation of the thyroid treatment.

Dr. Orías reported the results of experiments on normal and partially pancreatectomized rats. Subtotal pancreatectomized rats which conserve 5 per cent of pancreatic tissue tolerate the first diabetogenic dose of alloxan better than normal rats. The latter tolerate repeated subthreshold doses of alloxan with intervals of ten days between the injections, whereas subtotally pancreatectomized rats develop diabetes with relatively small doses of alloxan.

Medical Care in Boarding Schools

A law was recently passed by the executive government under which the heads of boarding schools are compelled to give attention to the physical and mental development of the children in the schools. The law provides that schools shall have clinical departments with a physician and a nurse; proper preventive and curative dental care will be given to the children; they will have four daily meals, which will be prepared in accordance with dietetic standards of the National Department of Public Health. Infractions will be punished by closing the offending schools.

Cultivation of Digitalis

Digitalis purpurea grows as a native plant in several regions of Argentina. Up to now, several pharmacists have taken the plant free of any cost for preparation of the pharmaceutical product for sale. The government is now in charge of the preservation and cultivation of the plant on a large scale. Free use of the plant is forbidden. The seeds of the plant hereafter will be harvested by the government and distributed to pharmacists.

Clinics for Heart Diseases

A polyclinic for heart diseases was recently opened to the public as a department of the Faculty of Medicine of the University of Buenos Aires. The building was constructed and properly equipped with a donation of $62,000 from the Virginio F. Grego foundation. The foundation will contribute $10,200 a year to the support of the polyclinic. The University of Buenos Aires will also provide funds for expenses.

Brief Items

Dr. Enrique A. Boero, gynecologist of Buenos Aires, former professor of gynecology and obstetrics of the Faculty of Medicine of Buenos Aires and an active worker in social medicine, died recently at the age of 64 years.——Dr. Arturo Mo, a well known psychiatrist of Buenos Aires, died recently at the age of 62 years.

The General Department of Penal Institutions of Argentina is negotiating with the government to increase the amount of money allowed for food in prisons.

The date of celebration of the second Pan American Congress of Ophthalmology was postponed from November 1944 to November 1945. The congress will be held in Montevideo. Pan American ophthalmologists are requested to send the annual dues to insure uninterrupted reception of the journal *Ophthalmologia Ibero Americana,* which is the official organ of the congress.

Dr. Juan Carlos Llames Massini, professor of obstetrics of the Faculty of Medicine of Buenos Aires, died recently in Buenos Aires.

Marriages

WILLIAM L. AINSWORTH, Bay Springs, Miss., to Miss Dorothy Alford of Crystal Springs in Charlottesville, Va., September 1.

JOSEPH PEDEN BAILEY to Miss Louise King Howe, both of Rock Hill, S. C., in Flat Rock, N. C., September 16.

JAMES NELSON HADDOCK, Cape Girardeau, Mo., to Miss Dorothy Mae Vaughan in Toledo, Ohio, June 8.

THOMAS DOYLE GHENT, Lancaster, S. C., to Miss Lydia Epps of Kingstree in Summerville, September 15.

JOHN EDWARD GILLICK, Clayton, N. Y., to Miss Ruth Catherine McGovern of New York, October 14.

JAMES YOUNG GRIGGS, Asheville, N. C., to Miss Betty Lee DeBusk in Winston-Salem, September 26.

THOMAS S. BROWNELL, Cleveland, to Miss Mary Miller of Mogadore, Ohio, in Akron, October 7.

GORDON L. NELIGH JR., Grand Island, Neb., to Dr. ROSALIE EVA BREUER of Lincoln, September 28.

EDWARD C. WOLSTON, Springfield, Mass., to Miss Maxine L. Askey of Oil City, Pa., September 28.

COSME JOSE FERRAIOLI, Santurce, Puerto Rico, to Miss Marjorie Whelan of New York recently.

LEROY B. DENNIS JR., Florence, S. C., to Miss Mary Emily Hinnant of Columbia, October 21.

LESTER J. CANDELA, Brooklyn, to Miss Margaret O'Keefe of Litchfield, Minn., recently.

JOHN MASSEY COBB, Tuskegee, Ala., to Miss Octavia Sadler of Birmingham, October 24.

Deaths

Charles Morton Rosenthal ✠ Brooklyn; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1934; fellow of the American College of Surgeons; member of the Brooklyn Ophthalmological Society; specialist certified by the American Board of Otolaryngology; assistant ophthalmologist at the Long Island College Hospital and clinical assistant ophthalmologist at the dispensary and senior clinical assistant ophthalmologist at the Brooklyn Eye and Ear Hospital; died in the New York Post-Graduate Medical School and Hospital, New York, September 1, aged 35, of subacute bacterial endocarditis.

Griffin Anderson Allen, Boston; Meharry Medical College, Nashville, Tenn., 1913; died August 5, aged 68, of arteriosclerotic heart disease and obesity.

Max Bacharach, Maryland, N. Y.; Julius-Maximilians-Universität Medizinische Fakultät, Würzburg, Bavaria, Germany, 1920; died September 12, aged 49, of chronic nephritis.

James Reginald Bailey ✠ Keysville, Va.; Medical College of Virginia, Richmond, 1926; on the associate staff of the Southside Community Hospital, Farmville; died September 13, aged 43.

William Thomas Barnette, Springfield, Ky.; Kentucky School of Medicine, Louisville, 1900; died in Shelbyville September 23, aged 70.

Thompson Mitchel Berry, Baton Rouge, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1908; died in Our Lady of the Lake Sanitarium September 20, aged 65.

Howard Black ✠ Palo Alto, Calif., Starling Medical College, Columbus, Ohio, 1896; member of the Pacific Coast Oto-Ophthalmological Society; died September 21, aged 70, of heart disease and generalized arteriosclerosis.

Jacob Peter Bottenhorn, Sigel, Pa.; Ohio Medical University, Columbus, 1904; died in the Warren State Hospital, Warren, July 12, aged 66, of carcinoma of the prostate.

Harry Maxwell Box ✠ Coral Gables, Fla.; Miami Medical College, Cincinnati, 1907; member of the Ohio State Medical Association; fellow of the American College of Surgeons; for many years practiced in Cincinnati, where he had been police and fire surgeon, and on the staff of the Deaconess Hospital; died September 30, aged 60, of coronary heart disease.

William Gerald Brymer, Bandera, Texas; College of Physicians and Surgeons, Dallas, 1905; also a pharmacist; past president of the Medina-Uvalde-Maverick-Val Verde-Edwards-Real-Kinney-Terrell-Zavala Counties Medical Society; served on the staff of the Santa Rosa Hospital, San Antonio; while practicing in Dewar, Okla., served as chief surgeon of the Consolidated Fuel Company; examiner for the Selective Service System; member of the Lions Club; died August 12, aged 72, of heart disease.

Thomas Henry Burke, Pittsburgh; Georgetown University School of Medicine, Washington, D. C., 1929; served an internship at the Pittsburgh Hospital; died July 2, aged 49, of coronary occlusion.

Arthur Alphonsus Chenay, Washington, D. C.; Detroit College of Medicine, 1897; veteran of the Spanish-American War and World War I; medical consultant for the National Rehabilitation Committee of the American Legion for many years; died September 17, aged 68, of coronary artery disease.

Lucie A. Hemenway Cook, Bloomington, Calif.; Northwestern University Woman's Medical School, Chicago, 1897; died September 25, aged 74.

Walter C. Crysler ✠ Littleton, Colo.; Harvey Medical College, Chicago, 1901; for many years county physician; served as mayor of Littleton; on the staffs of the Mercy Hospital and the Porter Sanitarium and Hospital, where he died August 4, aged 74, of coronary thrombosis.

Grant W. Curless, Beloit, Wis.; Atlanta College of Physicians and Surgeons, 1900; served during World War I; died August 27, aged 69, of coronary heart disease.

Bernard Charles Dorset, La Crosse, Wis.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; served during World War I; formerly practiced medicine in Denver, where he had been on the staffs of the Children's, St. Luke's, Presbyterian, Denver General, Colorado General and St. Joseph's hospitals; died November 1, aged 67, of coronary thrombosis and diabetes mellitus.

George G. Fitz, Bancroft, Idaho; State University of Iowa College of Medicine, Iowa City, 1898; member of the American Medical Association; served as vice president of the Pocatello Medical Society; served during World War I; died in Salt Lake City, September 25, aged 72, of cerebral hemorrhage.

Ralsa Marshal Fuller, Greenwood, S. C.; University of Georgia Medical Department, Augusta, 1899; member of the American Medical Association; served during World War I; died at the Greenwood Hospital September 28, aged 68.

Everett Rush Gose, Fayette, Mo.; Barnes Medical College, St. Louis, 1907; died August 21, aged 63, of heart disease.

Homer Wilford Gough, San Antonio, Texas; University of Texas School of Medicine, Galveston, 1915; member of the American Medical Association; at one time on the staff of the Southwestern Insane Asylum; died September 21, aged 62, of heart disease.

Charles A. Hadsell, Alamosa, Colo.; Missouri Medical College, St. Louis, 1885; associate member of the Colorado State Medical Society; honorary member of the Alamosa County Medical Society; died September 3, aged 90, of myocarditis.

Sherman Blaine Hibbard, Kansas City, Mo.; Rush Medical College, Chicago, 1912; member of the American Medical Association; died in Rochester, Minn., September 21, aged 56, of general peritonitis and leiomyoma of the stomach.

Robert Samuel Jacobs ✠ Washington, D. C.; Medical College of Virginia, Richmond, 1930; died in the Laurel Sanitarium, Laurel, Md., July 12, aged 39.

Harry Charles Kendig ✠ Mount Joy, Pa.; Jefferson Medical College of Philadelphia, 1930; served an internship at the Washington Hospital, Washington; member of the Rotary Club; died September 20, aged 41.

Cornelius C. Kepler, Pocahontas, Iowa; Chicago College of Medicine and Surgery, 1913; died September 3, aged 55, of carcinoma of the prostate.

Jesse Arthur King ✠ Elaine, Ark; University of Arkansas School of Medicine, Little Rock, 1918; medical director of the Elaine Hospital; surgeon for the Missouri Pacific Railroad; died in Monterey, La., August 7, aged 57, of pulmonary tuberculosis.

Robert Harrison Kistler ✠ Lansford, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1915; served during World War I; at one time chief surgeon for the Lehigh Coal and Navigation Company; formerly on the staffs of the Pennsylvania and Wills hospitals in Philadelphia; member of the police commission and a director of the First National Bank; died in the Coaldale State Hospital, Coaldale, October 4, aged 55.

William Russell Lightbody, Manchester, N. H.; Harvard Medical School, Boston, 1910; died in Boston August 11, aged 62, of cerebral arteriosclerosis.

William W. Livingston, Dunlo, Pa.; Eclectic Medical Institute, Cincinnati, 1902; member of the American Medical Association; served as a lieutenant in the medical corps of the U. S. Army during World War I; medical inspector in his school district for many years; died September 2, aged 72, of heart disease.

Frank William Maier, Medical Lake, Wash.; Beaumont Hospital Medical College, St. Louis, 1892; member of the American Medical Association; formerly health officer of Rocky Ford, Colo.; resident physician, Eastern State Custodial School, where he died August 16, aged 79, of coronary heart disease.

Jerome C. Malone, Faunsdale, Ala.; Memphis (Tenn.) Hospital Medical College, 1901; member of the American Medical Association; died September 26, aged 66, of heart disease.

Charles N. Martin, Warren, Ark.; Medical Department of Tulane University of Louisiana, New Orleans, 1878; member of the American Medical Association; died September 7, aged 89, of senility and hiccup.

George Scott Martin ✠ Susanville, Calif.; University of Louisville Medical Department, Louisville, Ky., 1909; a major in the medical corps of the U. S. Army, serving in France and England during World War I; member of the American Association of Industrial Physicians and Surgeons; physician and surgeon for the Southern Pacific Railroad; city health officer; past president of the Rotary Club; formerly medical director and owner of the Riverside Hospital; died October 8, aged 57, of coronary occlusion.

Edgar Stanley Matthews, Bunkie, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1900; served as secretary and treasurer of the Avoyelles Parish Medical Society; for eight years mayor of Bunkie; formerly a member of the state board of health; local surgeon for the

Texas and Pacific Railway; died September 25, aged 71, of arteriosclerosis and bronchopneumonia.

Leon Jordan May, Anna, Ill.; Kentucky School of Medicine, Louisville, 1905; member of the American Medical Association; since July 1941 managing officer of the Anna State Hospital; died September 22, aged 68, of coronary occlusion.

Bernard William Meyer, Columbus, Ohio; Ohio Medical University, Columbus, 1897; died August 11, aged 80.

John Thomas Mize, Wallis, Texas; University of Nashville (Tenn.) Medical Department, 1898; while practicing in Bryan served as county health officer; died September 22, aged 72, of tumor of the lung.

Guilford Dudley Mottier, Patriot, Ind.; Miami Medical College, Cincinnati, 1900; died in the Good Samaritan Hospital, Cincinnati, September 28, aged 71, of coronary disease.

Hans P. Nielson, Des Moines, Iowa; Ensworth Medical College, St. Joseph, Mo., 1899; died September 25, aged 67, of hypertensive heart disease.

Ludwig John Oblazney, Simpson, Pa.; Jefferson Medical College of Philadelphia, 1935; member of the American Medical Association; served an internship at the Allentown Hospital, Allentown, on the staff of St. Joseph's Hospital, Carbondale, where he died August 15, aged 35, of acute dilatation of the heart.

Charles Palen, Dubuque, Iowa; Northwestern University Medical School, Chicago, 1902; died September 30, aged 65, of pulmonary edema.

Jacob Allen Patton, Los Angeles; Rush Medical College, Chicago, 1890; retired in 1933 as medical director and second vice president of the Prudential Life Insurance Company, Newark, N. J., after thirty-eight years of service; formerly vice president and president of the Association of Life Insurance Medical Directors; assistant professor of chemistry, materia medica and genitourinary surgery at his alma mater from 1893 to 1908; died September 25, aged 77, of heart disease.

William Otto Pauli ✠ Cincinnati; Johns Hopkins University School of Medicine, Baltimore, 1907; a member of the medical staff of the Union Central Life Insurance Company since 1910, serving as assistant medical director from 1911 to February 1942, when he was elected associate medical director; at one time demonstrator in clinical microscopy at the Medical College of Ohio; died September 16, aged 62.

Robert Lee Payne, Monroe, N. C.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; served during World War I; died September 7, aged 57, of coronary occlusion.

Samuel Edward Peden, Perryville, Mo.; Barnes Medical College, St. Louis, 1910; served during World War I; died in the Veterans Administration Facility, Jefferson Barracks, September 2, aged 63, of generalized arteriosclerosis and cerebral thrombosis with left hemiplegia.

C. P. Perkins, Batesville, Miss.; Louisville Medical College, Louisville, Ky., 1903; died in St. Joseph's Hospital, Memphis, Tenn., October 9, aged 67, of ruptured gastric ulcer.

Doctor Absalom Pettit, Vicksburg, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1906; member of the American Medical Association; died September 21, aged 60.

Norman W. Phillips ✠ Clear Lake, Iowa; State University of Iowa College of Medicine, Iowa City, 1887; an affiliate Fellow of the American Medical Association; served as health officer; died September 10, aged 85, of cardiovascular renal disease.

Harry Pomerantz ✠ Lancaster, Pa.; Medico-Chirurgical College of Philadelphia, 1909; attached to British Expeditionary Force during World War I; on the staffs of the Rossmere Sanatorium, St. Joseph's Hospital and the Lancaster General Hospital, where he died September 19, aged 57, of carcinoma of the stomach.

Alfred R. Poole, Milan, Mo.; Kentucky School of Medicine, Louisville, Ky., 1904; died September 3, aged 66, of chronic glomerulonephritis.

Frances Mary Preston-Brown, Los Angeles; Woman's Medical College of Pennsylvania, Philadelphia, 1941; served an internship at the Hospital of the Woman's Medical College of Pennsylvania, Philadelphia, and a residency in psychiatry at the New York State Psychiatric Institute and Hospital in New York; died suddenly, August 18, aged 40.

John Robert Priest Jr., Houston, Miss.; University of Tennessee College of Medicine, Memphis, 1937; member of the American Medical Association; formerly health director of Kemper, Clarke and Wayne counties; served an internship at the Morningside Hospital in Tulsa, Okla., and the City Hospital in Mobile, Ala.; died October 4, aged 32, of acute cardiac failure.

Gideon D. Quinn, Springfield, Mo.; Louisville Medical College, Louisville, Ky., 1896; died in South Bend, Ind., September 24, aged 76, of cerebral hemorrhage.

Robert Ramroth, Marion, Ohio; Western Reserve University Medical Department, Cleveland, 1895; member of the American Medical Association; died in the Mount Carmel Hospital, Columbus, September 2, aged 72, of adenocarcinoma of the ascending colon and coronary occlusion.

Howard Jarvis Reger, Vernon, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1902; member of the American Medical Association; died July 26, aged 74, of arteriosclerosis.

Conrad B. Rice, Louisa, Ky.; Hospital College of Medicine, Louisville, Ky., 1898; member of the American Medical Association; served as president and member of the board of directors of the Bank of Blaine; died in a hospital at Cincinnati, September 25, aged 70, of pneumonia.

PUBLIC HEALTH SERVICE

William Smith Bean ✠ Medical Director, U. S. Public Health Service, Washington, D. C.; University of Virginia Department of Medicine, Charlottesville, 1914; interned at the U. S. Marine Hospital, Baltimore; commissioned in the regular corps of the public health service in August 1915; served as medical officer on the Coast Guard Cutter *Androscoggin* and with Dr. Joseph Goldberger on pellagra investigations in cotton mill villages in South Carolina; during World War I did extracantonment work in that state; with the exception of a few temporary assignments, had devoted twenty years to the operation of U. S. Marine hospitals; served as executive officer of the Marine hospitals in New Orleans, New York City and Ellis Island; medical officer in charge of the Marine hospitals at Mobile, Ala., Pittsburgh, Norfolk, Va., and Baltimore; from June 1944 until his death he was chief of the Hospital Division, Bureau of Medical Services; died suddenly November 26, aged 54, of coronary thrombosis.

Edward Cranch Ernst ✠ Medical Director, U. S. Public Health Service, Washington, D. C.; Columbia University College of Physicians and Surgeons, New York, 1911; served an internship at the Southern Pacific Railroad Company Hospital in San Francisco; commissioned on Jan. 10, 1916, as assistant surgeon in the U. S. Public Health Service and immediately assigned to duty at the Marine Hospital in San Francisco; during 1917 served as medical officer on the U. S. Coast Guard Cutter *Bacr;* served at the San Francisco Quarantine Station in 1918 and later for three years in the Philippine Islands, where he gained considerable experience in smallpox, cholera and leprosy, serving as medical officer in charge of the San Lazaro Contagious Disease Hospital in Manila and as extracantonment officer for the Philippine National Guard; in 1921 was detailed to the Division of Industrial Hygiene in Washington, D. C., and New York City; for twelve years, beginning in February 1922, served as medical director to the U. S. Employees' Compensation Commission; in 1934 appointed assistant chief of the division of personnel and accounts at headquarters of the public health service; in 1938, at the request of Dr. Hugh S. Cumming, director, was made assistant director of the Pan American Sanitary Bureau, a position he had held at the time of his death and in which he traveled widely in Central and South America, working closely with Latin American health authorities in cooperative programs for the improvement of health conditions; member of the Royal Tropical Medical Society, American Public Health Association, Far Eastern Tropical Medicine Association, Association of Military Surgeons of the United States and the American Hospital Association; died suddenly November 3, aged 58, of coronary occlusion.

Joseph Esthner Robinson, Memphis, Tenn.; Memphis Hospital Medical College, 1911; member of the American Medical Association; served during World War I; formerly on the staff of the United States Marine Hospital; died September 28, aged 58, of coronary thrombosis.

Joseph William Robinson ✠ Lisbon, Ohio; Eclectic Medical College, Cincinnati, 1927; served during World War I; died September 21, aged 50.

James Alfred Rolls Jr., Washington, D. C.; University of Michigan Medical School, Ann Arbor, 1923; member of the American Medical Association; died October 5, aged 45.

Eli W. Rose, Hundred, W. Va.; College of Physicians and Surgeons, Baltimore, 1888; died September 29, aged 80.

Frank M. Rumsey, Conneautville, Pa.; Cleveland Homeopathic Medical College, 1903; died in the Meadville City Hospital, Meadville, July 8, aged 70, of carcinoma of the prostate and myocarditis.

Presley Bliss Russell, Carthage, Miss.; Memphis (Tenn.) Hospital Medical College, 1901; died in the Mississippi Baptist Hospital at Jackson September 25, aged 65.

Olaf Halvard Rystad, Grand Forks, N. D.; Chicago College of Medicine and Surgery, 1913; member of the American Medical Association; on the staff of the Deaconess Hospital; died at Lake Plantaganet, Bemidji, Minn., August 16, aged 68, of coronary thrombosis.

Abraham S. Sanders, Brooklyn; Denver and Gross College of Medicine, 1903; member of the American Medical Association; formerly on the staffs of the New York Post-Graduate, Mount Sinai, St. Mark's and People's hospitals, all in New York; died in the Queens General Hospital, Jamaica, July 28, aged 66, of heart disease.

Charles William Schery ✠ St. Louis; St. Louis College of Physicians and Surgeons, 1904; formerly assistant to chair of histology, pathology and bacteriology at his alma mater; for many years city pathologist and bacteriologist; died in the Lutheran Hospital, September 9, aged 67, of generalized carcinomatosis.

Stuart Harris Sheldon ✠ Portland, Ore.; Rush Medical College, Chicago, 1902; fellow of the American College of Surgeons; served during World War I; chief, obstetric service, Salvation Army White Shield Home; on the staff of the Emanuel Hospital, where he died August 26, aged 68, of coronary thrombosis.

Frank Morton Sherman ✠ Newton, Mass.; Harvard Medical School, Boston, 1881; an Affiliate Fellow of the American Medical Association; died September 14, aged 87, of cerebral hemorrhage.

Henry Connelly Shurtleff, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1888; died in the Presbyterian Hospital, July 23, aged 80, of arteriosclerosis and diabetes mellitus.

Mark Harrison Smith ✠ Glendale, Calif.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1895; Rush Medical College, Chicago, 1898; died September 8, aged 73.

Samuel Reasin Wallis, Armour, S. D.; College of Physicians and Surgeons, Boston, 1900; member of the American Medical Association; county coroner; died August 30, aged 70, of heart disease.

Maria Constantine Walsh, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1893; member of the American Medical Association; died in the Jefferson Hospital July 1, aged 80, of auricular fibrillation and arteriosclerosis.

Capt. Roy E. Baze, M. C., A. U. S., 1910-1944

Capt. John S. Williams, M. C., A. U. S., 1909-1944

Lieut. Harold B. Thornburg (MC), U. S. Navy, 1911-1944

KILLED IN ACTION

Roy Ellis Baze, Chickasha, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1936; member of the American Medical Association; served an internship at the Hamot Hospital in Erie, Pa.; commissioned a first lieutenant in the medical corps of the Army of the United States on April 9, 1942; later promoted to captain; served in the African campaign before going to southern France, where he parachuted into occupied territory; awarded the purple heart posthumously; killed in action in France August 24, aged 34.

John Scott Williams, Ridgway, Pa.; Jefferson Medical College of Philadelphia, 1935; member of the American Medical Association; served an internship at the Methodist Episcopal Hospital in Philadelphia and the Burlington County Hospital, Mount Holly, N. J.; commissioned a first lieutenant in the medical corps, Army of the United States on May 12, 1942; later promoted to captain; awarded the Bronze Star Medal on July 26; killed in action in France August 14, aged 34.

Harold Babcock Thornburg ✠ Lieutenant (MC), U. S. Navy, Hollywood, Calif.; University of Southern California School of Medicine, Los Angeles, 1942; served an internship at the Naval Hospital, Bremerton, Wash.; commissioned a lieutenant (jg) in the medical corps of the U. S. Navy on July 5, 1942; was assigned to a South Pacific squadron after his completion of flight surgeon training in Pensacola, Fla.; promoted to lieutenant on May 1, 1943; killed in action at sea in the South Pacific area September 21, aged 33.

Bureau of Investigation

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the Federal Security Agency

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act, and in cases in which they refer to drugs and devices they are designated D.D.N.J. and foods, F.N.J. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the date of shipment; (4) the composition; (5) the type of nostrum; (6) the reason for the charge of misbranding, and (7) the date of issuance of the Notice of Judgment.]

Alterative Tonic Compound.—Hale Drug Company, Birmingham, Ala. Shipped Jan. 7, 1942. Composition: essentially methenamine, potassium iodide, a compound of iron, strychnine (0.01 grain per fluid ounce), extracts of plant drugs, including a laxative and an alkaloid-bearing one, with alcohol, sugar and water. Misbranded because label falsely represented that product was an efficacious alterative tonic, as well as a treatment for irritations caused by impurities of the blood, and would aid in the proper functioning of the bowels, kidney and bladder. Also misbranded because fabricated from two or more ingredients, whereas label failed to declare common or usual names of these, or the quantity of strychnine present.—[*D.D.N.J., F.D.C. 809; December 1943.*]

Bi-Lets.—Bi-Lets, Inc., Nashville, Tenn. Shipped March 10, 1942. Composition: essentially calomel, aloe and bile. Misbranded because, though a laxative, it was not labeled with the warning that it should not be taken in cases of nausea, vomiting, abdominal pain or other symptoms of appendicitis, and further, label failed to warn that frequent or continued use might result in dependence on laxatives.—[*D.D.N.J., F.D.C 810; December 1943.*]

Blue Ridge Mountain Mineral.—Robert T. Sides, trading as the C. S. & W. Mineral Company, Kannapolis, N. C. Shipped Feb. 21, 1941. Composition: a natural mineral which, when prepared according to directions on label, consisted essentially of a dilute solution of ferric sulfate, with minute amounts of sulfates of other minerals and some ferric hydroxide in suspension. Misbranded because label falsely represented that it was an effective treatment for high blood pressure, pellagra, nervous indigestion, rheumatism, kidney, bladder and stomach disorders, hemorrhoids, blood poison, female complaints and many other things.—[*D.D.N.J., F.D.C. 823; December 1943.*]

Bowel Regulator.—Hale Drug Company, Birmingham, Ala. Shipped Jan. 7, 1942. Composition: essentially compounds of sodium, potassium, magnesium and iron, tartrates, carbonates, and extracts of plant drugs, including a laxative and an alkaloid-bearing drug, with sugar and water. Misbranded because label failed to give adequate directions for use of this product as a laxative, and the directions given provided for no limitation as to duration of use. Further misbranded because labels failed to warn adequately that a laxative should not be taken in cases of nausea, vomiting, abdominal pain or other symptoms of appendicitis, and that frequent or continued use might result in dependence on laxatives to move the bowels. Further misbranded because label falsely represented that product would efficaciously regulate bowels and stomach and neutralize an acid condition of the body. Misbranded again because fabricated from two or more ingredients, whereas label failed to state common or usual names of said ingredients. Misbranded finally because label failed to bear accurate statement of quantity of contents.—[*D.D.N.J., F.D.C. 809; December 1943.*]

Cos-Tal Big C.—Alvin M. Hitt, trading as Cos-Tal Laboratories Company, Savannah, Ga. Shipped Oct. 7, 1941. Composition: an aqueous emulsion containing volatile oils, including oil of sandalwood, and resins. Misbranded in that the label statement: "Big C is indicated in cases of unnatural discharges" was false and misleading in representing that the product would be efficacious in the cure, mitigation, treatment or prevention of unnatural discharges, whereas it would not.—[*D.D.N.J., F.D.C. 825; December 1943.*]

Malitrate F-I.—W. Warren Walters and Organic Laboratories, Inc., Los Angeles. Shipped Dec. 8, 1941. Composition: concentrated apple juice. Misbranded because labels represented that the product was efficacious in the cure, mitigation, treatment and prevention of disease, by reason of the alkalizing properties of its components; that it was of value in preventing or treating gastrointestinal disorders, intestinal toxemia, diarrhea, various forms of nausea, and a good many other things.—[*D.D.N.J., F.D.C. 827; December 1943.*]

Special Formula 833.—Brewer & Company, Inc., Worcester. Mass. Shipped June 13, 1941. Composition: shown by biologic examination to contain approximately 1 milligram (333 International units) of vitamin B_1 (thiamin chloride) per tablet. Misbranded because of misleading label representation that the product would constitute an adequate or effective treatment for vitamin B_1 deficiency which might cause constipation, loss of vigor, various nervous and other important symptoms, or would be of special value for elderly men and women, as claimed.—[*D.D.N.J., F.D.C. 784; September 1943.*]

Correspondence

A COMPREHENSIVE BLOOD EXAMINATION FOR CLINIC ROUTINE

To the Editor:—Physicians working in general medicine in busy public clinics can be aided considerably by having in hand at the first visit of the patient as much routine laboratory data as is practicable. At the New York Dispensary we have found it possible, with small cost in time and effort, to determine the hemoglobin, the plasma protein and the erythrocyte sedimentation rate at the first visit of new patients by utilizing a portion of the blood withdrawn for the Wassermann test and employing the new density technic for hemoglobin and plasma protein and a concurrent sedimentation rate determination. The density method was devised last year by Dr. Phillips and others at the Rockefeller Institute for Medical Research. Devised especially for the use of medical units in our armed forces, it has proved to be admirably adapted for use in busy civilian clinics. It is accurate, requires the minimum of time and skill and calls for no special apparatus. The method as yet has not been described by its authors, but a description can be found in Peters and Van Slyke's "Quantitative Clinical Chemistry—Methods," 1943 edition, and in Kolmer's "Clinical Diagnosis by Laboratory Methods," 1944 revised edition.

For clinic use I have found the following plan satisfactory: The new patient, except in trivial cases, is sent from the admission interview direct to the nurse who collects blood for the Wassermann test. An extra 3 cc. of blood is withdrawn and placed in a 10 cc. vial charged with oxalate. The examination is then made by the nurse, or the specimen is sent to the laboratory or to the consulting room of the physician. The examination is so easy that the physician himself can complete it without serious interruption of his clinical work. The final step in the examination is made at the end of one hour, or after a half hour if approximate results are sufficient.

This comprehensive blood examination at the first visit has definite advantages. There is less psychologic resistance on the part of the patient than is occasioned by the Wassermann test alone, for he is told that the examination is for general information about his blood. But the chief advantage is that the results obtained indicate to the clinician at the first visit many of the cases of concealed infection or of anemia and thus aid him suitably to apportion his time between the more and the less serious cases.

FREDERICK H. HOWARD, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: New York, June 8-9. Final date for filing application is March 12. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Feb. 19. Final date for filing application is Dec. 15. Asst. Sec., Dr. W. A. Werrell, 1301 University Ave., Madison 5, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Spring. Final date for filing application is Feb. 1. Sec., Dr. Paul C. Bucy, 912 S. Wood St., Chicago 12.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 3. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: New York, June 13-16; Chicago, Oct. 3-6. Final date for filing application is Jan. 1. Sec., Dr. S. Judd Beach, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 5-8. Chicago, Oct. 3-6. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City, Ia.

AMERICAN BOARD OF PEDIATRICS: *Oral.* New York, April 14-15. Final date for filing application is Dec. 15. Chicago, May 19-20. Final date for filing application is Jan. 19. Sec., Dr. C. A. Aldrich, 115½ First Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* New York, June 3. Final date for filing application is May 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Revocation of License for Performance of Nontherapeutic Abortions.—After notice and hearing the State Board of Health of Mississippi revoked Johnson's license to practice medicine in Mississippi on the ground that he had procured an abortion not necessary to preserve the life of a pregnant woman, which is a cause for the revocation of a license under the Mississippi medical practice act. The physician, by a writ of certiorari, brought the matter for review before the circuit court, Hinds County, which reversed the order of the board and remanded the cause for further procedings. The board then appealed to the Supreme Court of Mississippi.

The physician contended first that the proceedings by which his license was ordered revoked by the board were not lawfully initiated. He argued that the state of board of health took no action itself prior to the hearing, that the alleged notice served on him was initiated solely by the executive officer of the board without the authority of the board and that since no charge against him had been lodged with the board the proceedings instituted were unauthorized and illegal. The notice of the proceedings served on the physician, said the court, was in the form of a registered letter and was signed by the secretary and executive officer of the board, had attached thereto the seal of the board, and notified the physician to appear before the board at the time and place named therein for a hearing on the charges therein set out. The notice purported to be sent by the authority and direction of an order of the executive committee of the board, adopted at a called meeting Oct. 6, 1943, at which only two of the members of the committee were present, the order reciting that certain complaints and grievances against the physician had been made known to the committee. The state board of health, continued the court, by statute, consists of ten members. Nine of those members are appointed by the governor, eight to be licensed physicians and one to be a licensed dentist. The tenth member, apparently, is elected and is to be the executive officer and secretary of the board and is vested with all the authority of the board when it is not in session. The physician who signed the notice served on Johnson was the duly elected member of the board who lawfully was the executive officer and the secretary of the board. By statute the board is also authorized to appoint an executive committee of three members and, as stated in the statute:

> "Said executive committee shall have authority to execute all the powers herein vested in said board, in the interim of the meetings of said board; and any action of said executive committee shall be legal and binding until modified or annulled by said board of health. . . . Any two members of the executive committee shall be a quorum for the transaction of business." (Code 1942, Section 7027).

Further, said the court, by Section 8893, supra, the board "may on its own initiative or on complaint suspend or revoke for any cause named below [including the cause alleged as the basis for the action against Johnson] any license" of a physician licensed to practice in Mississippi. Thus it is seen that the executive committee can legally act through two of its members, that the action of that committee and the issuance of the notice to Johnson were the valid acts of the board itself and that no complaint, formal or otherwise, to either the board or the committee is essential to the lawful initiation of the proceedings by the board.

The physician next contended that the notice of the charges given him in the proceedings was not legally sufficient in substance in that the charges set out in the notice were vague, general, indefinite and inconsistent and did not inform him of the nature and cause thereof so that he could prepare his defense, thus denying him his constitutional right of due process of law. The notice, answered the court, served on Johnson described the charges against him as "Procuring, or attempting to procure, or pretending to procure, an abortion that is not necessary to preserve the life of a pregnant woman." This was in the exact language of the statute (Section 8893 (a) (5), supra) and the wording of the order of the executive committee authorizing and directing its issuance. Following the receipt of this notice by Johnson his counsel wrote the board requesting that he be furnished with the cause and nature of the accusation. In reply counsel for the board wrote Johnson's counsel, giving him the names of ten women on whom "unnecessary abortions" had been procured by Johnson with the approximate times when such acts were performed. Construing the original notice and this letter together, they charged, in the last analysis, that Johnson, at different times approximately stated, had procured abortions on ten named pregnant women, which abortions were not necessary to preserve their lives. This eliminated the alternatives of attempting or pretending to procure or aiding or abetting in procuring such abortions set out in the original notice. Was this sufficient to give the physician notice of the nature and cause of the offense? Mississippi has no statute prescribing the form and substance of such notices. The statute does define the offense, as previously noted, and the original notice here was in the words of the statute which itself is usually sufficient, even in criminal charges. However, the essentials of such notices, in the absence of statutes prescribing them, seem well settled. As was said by the Supreme Court of Florida in *State* v. *Whitman*, 116 Fla. 196, 150 So. 136:

> "And in such proceedings it is sufficient if the accused is informed with reasonable certainty of the nature and cause of the accusation against him, has reasonable opportunity to defend against attempted proof of such charges, and the proceedings are conducted in a fair and impartial manner, free from any just suspicion or prejudice, unfairness, fraud, or oppression."

Further as stated in 41 Am. Jur. 184: "In the absence of statute requiring it, the strict rules of pleading in judicial cases do not apply to revocation proceedings before a board of medical examiners. . . ." It is recognized that the members of an administrative board such as a board of health or board of medical examiners are not learned in the law and legal proceedings and more laxity is allowed in their pleading and procedure than in strict law courts, provided that no substantive rights of the accused are denied him.

The accusation in this case, continued the court, informed the physician of every element involved in the charge except that it did not describe the means, nor technic used in producing the abortions, or undertake to give a definition thereof. It was not necessary to set out the means. Lacking lawful justification for the act, it mattered not whether it was done by giving medicine or using instruments—it was abortion. Nor was it material that the notice failed to define abortion. As was said in 1 Am. Jur. 133: "In criminal law the crime of abortion is the wilful bringing about of an abortion without justification or excuse." The only justification or excuse in this case would have been the necessity to save the lives of the women concerned. The charge says that was not necessary. Stripped of all technical niceties, and looked at in a common sense way, it would seem rather absurd to inform a physician that he had performed abortions not necessary to save the lives of the women and at the same time to assume that he did not know the meaning of the word abortion and that he needed to be given a definition and a description of the detailed manner in which an abortion is produced. It is significant that the physician after receiving the additional information requested by his counsel proceeded with the hearing and without requesting further particulars, which, in civil actions, precludes such person from thereafter complaining as to a lack of knowledge of details. While this court is zealous to guard individual rights and would caution quasi judicial tribunals to be careful that such rights are fully protected in proceedings before them, yet it is clear in this case that the physician was informed with reasonable certainty of the nature and cause of the accusation against him, had ample opportunity to defend against them, and had a fair and impartial hearing.

The court, accordingly, reversed the judgment of the trial court and ordered reinstatement of the judgment or order of the state board of health revoking Johnson's license to practice.—*Mississippi State Board of Health v. Johnson, 19 So. (2d) 445 (Miss., 1944).*

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

68:157-230 (Sept.) 1944

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Significance of Complete Preventive Medical Program for Children. C. A. Aldrich.—p. 168.
Preparation and Immunizing Properties of Protamine Diphtheria Toxoid. V. Ross.—p. 172.
Congenital Anomalies of Lower Part of Rectum: Analysis of 16 Cases. M. J. Lee Jr.—p. 182.
Psychogenic Incontinence of Feces (Encopresis) in Children: Report of Recovery of 4 Patients Following Psychotherapy. E. Lehman. —p. 190.

American Journal of Hygiene, Baltimore

40:109-226 (Sept.) 1944

Results Obtained with Heat Killed Tubercle Bacilli Administered to Persons in General Population. C. W. Wells and E. W. Flahiff. —p. 109.
*Results Obtained in Man with Use of Vaccine of Heat Killed Tubercle Bacilli C. W. Wells, E. W. Flahiff and H. H. Smith.—p. 116.
Local Reactions Following Injection of Heat Killed Tubercle Bacillus Vaccine. C. W. Wells, E. W. Flahiff and H. H. Smith.—p. 127.
Effectiveness of Ultraviolet Irradiation of Upper Air for Control of Bacterial Air Contamination in Sleeping Quarters: Preliminary Report. R. Schneiter, A. Hollaender, B. H. Caminita, R. W. Kolb, H. F. Fraser, H. G. Du Buy, P. A. Neal and H. B. Rosenblum.—p. 136.
Detection of Vi Agglutinins in Sera of Typhoid Carriers. Ethalinda H. Brower.—p. 154.
Study of Reporting of Paralytic Poliomyelitis in Massachusetts, 1928-1941. N. B. Nelson and W. L. Aycock.—p. 163.
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Genus Flebotomus in California. O. Mangabeira, Filho and P. Galindo. —p. 182.
Some Epidemiologic Characteristics of Malaria in North Alabama as Determined by Data Collected over the Twenty Year Period 1923-1942. R. B. Watson and Margaret E. Rice.—p. 199.
Probably New Type of Nonmannitol Fermenting Shigella. Maud Gober, Virginia Stacy and Mary Woodrow.—p. 209.
Tests for Specificity of Tumors and Sera of Rats. G. H. Bailey and R. E. Gardner.—p. 212.
Efficiency of Intranasal Inoculation as Means of Recovering Poliomyelitis Virus from Stools. H. A. Howe and D. Bodian.—p. 224.

Results Obtained with Vaccine of Killed Tubercle Bacilli.—Wells and his associates report studies on the protective effect of heat killed tubercle bacilli against human tuberculosis conducted in the Mental Hospital, Kingston, Jamaica, over a period of more than ten years. The average annual patient population of the Kingston Mental Hospital approximated 2,500, with about 540 admissions each year. The number of patients dying from all causes per year averaged 260, and approximately 25 per cent of all deaths were due to tuberculosis. Among 434 persons with tuberculosis under observation during the study, only 61 (14 per cent) had clinical tuberculosis on admission; the remainder developed it while in the institution. Patients were permitted access to large compounds, one for each sex, where practically no restrictions were placed on their freedom of movement. The effect on the spread of tuberculosis of an arrangement of this kind in a population with a high incidence of open tuberculosis is apparent. Certainly the conditions presented a severe test for studies to determine the protective value of inoculations with a heat killed tubercle bacillus vaccine. The authors found significantly lower tuberculosis attack and death rates among recipients of heat killed tubercle bacilli administered intracutaneously than among persons alternately chosen but not vaccinated, who served as controls. The differences were greatest during the first two years of observation. The attack and death rates for tuberculosis among persons strongly positive to tuberculin on admission to an institution with a high tuberculosis prevalence were consistently and significantly lower than such rates in groups of persons containing weak and negative tuberculin reactors, vaccinated or controls. The results obtained in this study support the suggestion that there is a practical use for this or a similar heat killed tubercle bacillus vaccine in certain groups of individuals who may be subjected to unusual risk of tuberculous infection. Such groups might include medical students, pupil nurses, hospital attendants, household contacts and possibly others.

American Journal of Medical Sciences, Philadelphia

208:421-560 (Oct.) 1944

*Diagnosis of Hemorrhage in Man: Study of Volunteers Bled Large Amounts. H. A. Shenkin, R. H. Cheney, S. R. Govons, J. D. Hardy, A. G. Fletcher Jr. and I. Starr.—p. 421.
*Effect of Artificial Restriction of Activity on Recovery of Rats from Experimental Myocardial Injury. W. C. Thomas and T. R. Harrison.—p. 436.
*Alloxan Diabetes in Rabbit: Consideration of Morphologic and Physiologic Changes. O. T. Bailey, C. C. Bailey and W. H. Hagan. —p. 450.
Acute Yellow Atrophy of Liver in Early Syphilis: Case Report with Summary of Literature. Martha F. Leonard.—p. 461.
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Burn Trauma Precipitating Acute Leukemia or Leukemoid Condition. D. Weiss and K. E. Haines.—p. 490.
Use of an Agglutination Inhibition Test in Studying an Epidemic of Influenza. A. L. Florman and J. P. Crawford.—p. 494.
*Experimental Chronic Carb. Monoxide Poisoning of Dogs. F. H. Lewey and D. L. Drabkin.—p. 502.
Cardiac Changes from Carbon Monoxide Poisoning. W. E. Ehrich, S. Bellet and F. H. Lewey.—p. 511.

Diagnosis of Hemorrhage in Man.—Shenkin and his associates found that after operations in which much blood was lost some patients showed none of the signs ordinarily expected after profuse hemorrhage. They made observations on 18 volunteers who were bled approximately 500 cc. and on 17 who were bled about a liter. Estimations of pulse rate, blood pressure, venous pressure, cardiac output (ballistocardiograms) and hematocrit were made before and after the hemorrhage, during the recovery and often after replacement of the blood. Cardiac output diminished little after the loss of 500 cc. of blood; after the loss of a liter it regularly diminished significantly, and during syncopal attacks it diminished profoundly. After completion of the bleeding, the cardiac output slowly returned toward the value found before the hemorrhage. The effects of hemorrhage on healthy men may be divided into three stages of severity. In the first stage the subject is symptom free at rest and has a pulse rate and blood pressure within normal limits. On arising, acceleration of pulse rate and some diminution of blood pressure are found. In the second stage there are still no noteworthy abnormalities as long as the subject is recumbent and at rest, but the upright position cannot be tolerated and syncope soon overwhelms the subject if he arises. In the third stage syncopal attacks accompanied by bradycardia occur even though the subject is at rest and recumbent. The old concept that acute hemorrhage can be readily diagnosed by a rapid pulse and a low blood pressure is erroneous. Recumbent subjects may be bled to the point of collapse without exhibiting conspicuous tachycardia, and during the period of severe symptoms profound bradycardia is the rule. The blood pressure usually remains within the normal range until the symptoms of collapse begin, when it diminishes profoundly. Hemorrhages causing no signs or symptoms as long as the subjects are recumbent can be detected by having them sit or stand upright.

Effect of Restriction of Activity on Recovery of Rats from Myocardial Injury.—Thomas and Harrison say that, although rest in bed is the most widely used method of treatment of patients with acute myocardial disorders, there have been practically no well controlled clinical or experimental studies concerning its value and its limitations. Opinions vary widely about the length of time during which rest should be applied as well as regarding the strictness of the regimen of rest. The effect of exercise on animals with acute myocardial injury has been studied previously, but experimental attempts

at enforcing rest on animals has not heretofore been attempted. The authors review observations on a large number of rats in which experimental injury was produced by application to from three to five areas on the left ventricular surface of the head of a nail heated almost to redness. The mortality of these rats was decidedly greater when the animals were kept closely confined in small cages which restrict muscular activity. Animals so confined display considerably less activity, as measured by the work adder method, than control animals allowed to wander freely about in larger cages. Observations with the optional treadmill have shown that following injury to the heart the rat tends to return to the preoperative level of exercise within a period of three to seven days. Enforced strenuous muscular effort, even when carried out within twenty-four hours after cardiac injury, did not materially increase the mortality in rats. Likewise, such exercise carried out three or more days after the operation did not cause a significant increase in mortality. The authors point out that prolonged rest in bed following myocardial infarction in patients has serious disadvantages as well as some advantages. On the basis of the available evidence it would appear that during the first two weeks the advantages of strict bed rest probably outweigh the disadvantages but that after this time the reverse is probably true.

Alloxan Diabetes in Rabbits.—The Baileys and Hagan report pathologic findings in the pancreas and other organs of rabbits at varying intervals after the intravenous injection of alloxan. A single injection of a 5 per cent aqueous solution of alloxan was used. The total diabetogenic dosage was 200 mg. of alloxan per kilogram of body weight. Smaller doses were used for the production of transitory diabetes. Lesions induced by alloxan in the islets of Langerhans of the rabbit begin almost immediately after the injection and are degenerative from the beginning. Degenerative changes in the islet cells are already apparent in the initial hyperglycemic stages, while in the hypoglycemic stage they progress to a point where they approach those of the diabetic phase. The pancreatic acini remain normal throughout, and changes in organs other than the pancreas are minimal. The most striking characteristic of the lesion is its specificity for the islets of Langerhans. The beta cells are affected most severely, while a certain percentage of the alpha cells remain intact. From the point of view of the investigator it is unfortunate that the alpha cells are not completely destroyed. There are conspicuous species differences in the extent of extrapancreatic lesions induced by the injection of alloxan. The lesions of the kidney in the rat are much more severe than those in the rabbit. The lesions induced by small doses of alloxan are very striking. They resemble more the sequences produced in other organs following administration of certain carcinogenic hydrocarbons than the lesions produced by massive doses of alloxan or those recognized in human diabetes. Injection of alloxan not only provides a useful technic for obtaining diabetic animals in the laboratory and for the study of diabetic complications but also provides a useful technic for the study of numerous problems in general pathology.

Experimental Chronic Carbon Monoxide Poisoning of Dogs.—The U. S. Department of Labor sets the limit of safe concentration of carbon monoxide in air in industrial plants at 0.01 volume per cent (100 parts per million). Lewey and Drabkin state that the amount of carbon monoxide combined with hemoglobin varies greatly even with the same exposure. A person exposed continually for some months to the same carbon monoxide concentration in air may, supposedly by adaptation, show a gradual decrease in the percentage of carbon monoxide hemoglobin. Hence, safety limits given in terms of carbon monoxide concentration in air give only an approximate idea of the toxicity relationships of the gas in the body. The value of 0.01 volume per cent carbon monoxide in air leads theoretically in man to approximately 16 per cent carbon monoxide hemoglobin. By agreement of the safety engineers of the U. S. Army the upper permissible limit is set at 20 per cent carbon monoxide hemoglobin. Dogs exposed for five and one-half hours a day, six days a week, over eleven weeks, to an atmosphere containing 0.01 volume per cent of carbon monoxide and reaching daily 20.1 ± 1.1 per cent of carbon monoxide hemoglobin showed a consistent disturbance of postural and position reflexes and of gait. Some of them showed a pathologic electrocardiogram characteristic of anoxia and necrosis of single heart muscle fibers. Their central nervous systems showed, three months after termination of the experiment, microscopic changes in the cortex and white matter of the cerebral hemispheres, in the globus pallidus and in the brain stem. These alterations corresponded in type and localization to those found in acute carbon monoxide poisoning but were smaller, more scattered and less destructive. They followed in their arrangement the course of the blood vessels, the walls of which were only occasionally damaged. One dog, in which the posterior coronary artery had been ligated one year prior to the exposure for a period of only eighteen days to carbon monoxide, showed the earliest and severest cardiac and cerebral changes of all animals. This suggests that an inadequately functioning heart increases the general risk in carbon monoxide poisoning and may be responsible for a higher degree of brain damage. Chronic carbon monoxide intoxication may occur in dogs at carbon monoxide concentrations which have been regarded as within the safety limits for man. These experiments do not permit conclusions about potential human reactions to the same conditions.

American Journal of Physiology, Baltimore

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Blood Picture of Iron and Copper Deficiency Anemias in Rabbit. S. E. Smith, Mary Medlicott and G. H. Ellis.—p. 179.
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Changes in Phosphate of Muscle During Tourniquet Shock. J. L. Bollman and Eunice V. Flock.—p. 290.

Work in Heat as Affected by Intake of Water, Salt and Glucose.—Pitts and his collaborators investigated the effects of water, salt, glucose and water soluble vitamins on 6 healthy, fully acclimatized young men. The best performance of fully acclimatized young men on a good diet, performing intermittent hard work in the heat, was achieved by replacing hour by hour the water lost in sweat. Considerably less than this amount of water led in a few hours to a serious inefficiency and eventually to exhaustion. The replacement of salt hour by hour had no advantage. Replacement of salt loss meal by meal was adequate. Administration of glucose proved of little or no value when compared with the great benefit of large amounts of water. There was no advantage from administering 200 mg. of ascorbic acid, 20 mg. of thiamine hydrochloride, 20 mg. of riboflavin or large doses of brewers' yeast, either singly or together either during work or the day before. Water transport and supply are sometimes difficult, but when water is available it should not be forbidden on the traditonal ground that during work it is bad for one. Men should be encouraged to drink to capacity. When a good daily diet is not available because of failure of supply or is not eaten because of ignorance or anorexia, which is so common in hot environments, it is desirable to ensure adequate intake at least of salt, by means of salted drinking water or tablets, and probably of vitamins by means of concentrates.

American Journal of Public Health, New York

34:931-1048 (Sept.) 1944

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*Epidemic of 3,000 Cases of Bacillary Dysentery Involving a War Industry and Members of Armed Forces. C. H. Kinnaman and F. C. Beelman.—p. 948.
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Tomorrow's Opportunities in Tuberculosis Nursing. Dorothy Deming.—p. 957.
Problem of Control of Tuberculosis in Mental Hospitals with Reduced Personnel. G. W. Weber, R. E. Plunkett and F. MacCurdy.—p. 962.
Health Education in Nutrition: Adapting Business Promotion Technics to Public Health Education. Annabelle Desmond and Leona Baumgartner.—p. 967.
Gonorrhea Contacts: Criteria for Management. J. H. Lade.—p. 974.

Epidemic of Bacillary Dysentery.—Kinnaman and Beelman describe an epidemic of bacillary dysentery that occurred in Newton, a town with a population of 11,000 in southeastern Kansas. Samples taken from the deep wells showed no contamination, but those from various points on the distribution system were heavily contaminated. A bit of information which proved of extreme importance was received from a Santa Fe Railway water department employee who said that a sewer block had occurred at a Mexican village on the southwest outskirts of the city about the time that dysentery cases developed in the city. Contrary to previous statements by city officials that no change had been made to the distribution system, further information uncovered the fact that changes had been made on the two main supply lines entering the city at a point close to this Mexican village. Investigation showed that a service connection came from a main to the Mexican villages. The situation was reconstructed as follows: When the water pressure was off on September 7 and 8, persons in the village attempting to get water apparently opened the valves and, not obtaining water, left them open; this in turn allowed the sewage backed up in the box to flow through the drain opening into the water main. The epidemiologic investigation revealed that the peak onset occurred on September 10, with 743 persons giving this date as the beginning of their sickness. As a result of the epidemic, business in the city was practically at a standstill on Thursday, September 10, when it is estimated about 2,000 persons were ill. Laboratory examination showed the predominating organism recovered from the stools of sick persons and from the intestinal mucosa in fatal cases to have been Shigella paradysenteriae, Flexner group. The water supply of Newton also supplies all passenger coaches of the Santa Fe Railroad. There were 2,871 regular passenger cars (Pullman and coaches) supplied with water between the dates of September 3 and the afternoon of September 14. From scattered cases traceable to Newton, it is assumed that there were many cases other than those occurring in the city. A great number of war workers were absent from their jobs for several days; an unknown number of soldiers and civilians were infected; the ordinary business of the city was disrupted for three days. Later, important transcontinental trains, many of them troop trains, were delayed an average of one hour while taking water at a nearby safe supply. With institution of proper public health protection measures the epidemic quickly subsided.

Archives of Ophthalmology, Chicago

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Journal of Experimental Medicine, New York

80:257-340 (Oct.) 1944

Comparative Effects of Vitamin B_1 Deficiency and Restriction of Food Intake on Response of Mice to Lansing Strain of Poliomyelitis Virus, as Determined by Paired Feeding Technic. Claire Foster, J. H. Jones, W. Henle and Frieda Dorfman, with technical assistance of Mabel E. Quinby and Dorothy L. Alexander.—p. 257.
*Studies in Human Immunization Against Influenza: Duration of Immunity Induced by Inactive Virus. G. K. Hirst, E. R. Rickard and W. F. Friedewald.—p. 265.
Relation of Chemical Structure in Catechol Compounds and Derivatives to Poison Ivy Hypersensitiveness in Man as Shown by Patch Test. H. Keil, D. Wasserman and C. R. Dawson.—p. 275.
Essential Difference Between Two Optimum Proportions Flocculation Ratios. W. C. Boyd and Marjorie A. Purnell.—p. 289.
Preparation of Type Specific Polysaccharide of Type I Meningococcus and Study of Its Effectiveness as Antigen in Human Beings. E. A. Kabat, Hilda Kaiser and Helen Sikorski.—p. 299.
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Nutritional Requirements and Factors Affecting Production of Toxin of Clostridium Septicum. A. W. Bernheimer, with technical assistance of Margaret T. Spencer.—p. 321.
Kinetics of Lysis by Clostridium Septicum Hemolysin. A. W. Bernheimer.—p. 333.

Immunization Against Influenza.—Recent evidence on the effect of subcutaneous vaccination with influenza virus showed that the incidence of epidemic influenza was consistently reduced by about 75 per cent when the period between vaccination and an epidemic was short. Hirst and his associates present studies on a similar vaccine in which the period between vaccination and an epidemic was about one year. The PR8 strain of influenza A and the Lee strain of influenza B were used for the production of most of the vaccine. Penal institutions in five widely separated states of the Midwestern, Southern and Eastern United States were chosen for the study. These institutions offered obvious advantages for this type of work, since in each of the groups the medical care was good, there was adequate, readily available hospital space and there were full time physicians in attendance. Seven such institutions were studied. Administration to human beings of formaldehyde killed influenza virus, concentrated from allantoic fluid, resulted in a high order of antibody response within two weeks after injection. Even after one year the great majority of persons vaccinated had antibody levels considerably above their prevaccination titer for the PR8, Lee and a current 1943 strain. An investigation of the occurrence of epidemic influenza A in seven widely separated populations one year after vaccination of part of these groups showed that the attack rate among vaccinated persons was consistently lower than that of control individuals. The average reduction in the attack rate was of the order of 35 per cent.

Military Surgeon, Washington, D. C.

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*Cardiac Tamponade: Report of Stab Wound in Right Ventricle. W. J. Gillesby.—p. 284.
Value of Electrocardiogram in Acute Rheumatic Fever: Report of 3 Cases. P. P. Pease, L. G. Steuer and C. H. Peters.—p. 287.
Appendicitis: Study of Over 500 Cases Observed During Present Emergency in Army Hospitals. W. H. Gerwig Jr.—p. 291.
Diagnosis of Appendicitis with Gastroenteritis. W. H. Graham.—p. 296.
Reevaluation of Sulfa Drugs. C. Lyons.—p. 301.
Safety Factors in Use of Intravenous Anesthesia. J. D. Marco.—p. 305.
Erythema Multiforme Pluriorificialis (Stevens-Johnson Disease). B. D. Erger.—p. 308.
March Fractures: New Concept of Their Etiology and Logical Method of Treatment. L. W. Breck and N. L. Higinbotham.—p. 313.
Significance of Persistent Enuresis in History of Psychopathic Personality. J. J. Michaels.—p. 315.
Tannic Acid Fixative Method for Staining Protozoa. J. H. Alli.—p. 317.
Cancer in Armed Forces. W. G. Cahan.—p. 319.
Easily Made Suction Apparatus. P. W. Stumm.—p. 321.

Prophylactic Use of Sulfadiazine in Meningococcic Infection.—Painton states that approximately 18,000 men were given 2 Gm. of sulfadiazine at 1 p. m., 2 Gm. at 7 p. m. and 1 Gm. at 7 a. m., each man receiving a total of 5 Gm. in a

period of eighteen to nineteen hours. The only type of reaction noted was a skin eruption, which occurred in 6 cases. Up to eight weeks after the drug was ingested no man with meningococcic infection, either meningococcemia or meningococcic meningitis, has been been hospitalized since the first day the drug was administered; no case of scarlet fever has been diagnosed since the prophylactic administration of sulfadiazine. The incidence of upper respiratory infection was reduced by approximately 50 per cent for nine days following the administration of the drug. The incidence of contagious virus infection, as measles and mumps, was also reduced for one week following the ingestion of the drug. The results cannot be explained by better climatic conditions. The number of men appearing on sick call was reduced by approximately 33⅓ per cent for a period of eleven days following the ingestion of the drug.

Stab Wound in the Right Ventricle.—A soldier was stabbed in the left chest with a pocket knife. Two hours after the injury Gillesby found the patient cyanotic, cold and clammy. His pulse was barely perceptible and his blood pressure unobtainable. All superficial veins were distended. Cheyne-Stokes respiration was present. Heart sounds were muffled, and the apex beat could not be located. Physical findings revealed left pneumothorax. A diagnosis of cardiac tamponade and left pneumothorax was made. An incision was made over the sixth rib from the scapular line to the costochondral junction. The rib was exposed and subperiosteal resection planned. However, because the anesthetist stated that she could no longer feel a pulse, an intercostal incision was rapidly made and the ribs were separated manually. The lung was pushed aside and the pericardium palpated. A faint pulsation could be felt. The pericardium was widely incised, releasing a gush of clots. The heart began to beat violently, and blood could be seen coming from an incision in the right ventricle. A finger was placed on the hole and an apical suture applied. The time consumed from the beginning of the incision to this point was about two minutes. The pulse was better. The wound in the heart was closed with two silk sutures so placed as to avoid the coronary vessels. Bleeding was well controlled. The pericardial sac was cleaned of clots and the heart inspected. The extensive transpleural approach used is advocated as an "all purpose" incision. Hyperventilation was used to prevent pulmonary complications. The pericardium was left open in communication with the left pleural cavity to permit effusion to drain into the pleural cavity. Electrocardiographic tracings taken postoperatively showed only an inversion of the T wave in lead 4.

Missouri State Medical Assn. Journal, St. Louis

41:179-196 (Sept.) 1944

Venereal Disease Control in Missouri. R. R. Wolcott.—p. 179.
Barnard Free Skin and Cancer Hospital Research: Report for 1943. E. V. Cowdry.—p. 181.

41:197-214 (Oct.) 1944

Cardiac Disorders in Army General Hospital. J. T. King.—p. 197.
Special Problems of Poor Surgical Risks, Especially Age. W. B. Kountz.—p. 200.
Gastric and Duodenal Lesions. D. A. Williams.—p. 202.
Physiologic Management of Burns. V. T. Williams.—p. 205.

New Orleans Medical and Surgical Journal

97:151-196 (Oct.) 1944

Doctor and Socialized Medicine. W. R. Metz.—p. 151.
*Rabies: Ten Year Survey of Pasteur Institute of Charity Hospital of Louisiana at New Orleans. E. E. Palik and Emma S. Moss.—p. 153.
Care of Premature Infant at Charity Hospital. Hazel Pierce and W. Sako.—p. 163.
March Fracture in Industry. J. H. Eddy Jr.—p. 171.
Fracture of Patella: Analysis of 150 Cases at Charity Hospital. L. K. Loomis.—p. 173.
Value of Central Field Studies Over Conventional Type of Visual Field Studies. S. R. Gaines.—p. 176.
Incidence of Several Etiologic Types of Heart Disease in Charity Hospital. J. H. Musser and C. S. Dempsey.—p. 180.

Rabies.—Palik and Moss present an analysis of 12,237 patients admitted to the Pasteur Institute Clinic in New Orleans and of 3,003 animal brains submitted for examination and diagnosis during the period from Jan. 1, 1934 to Oct. 31, 1943 inclusive. The Pasteur treatment was given to 4,146 patients. Of 3,003 animal brains submitted for examination 1,003, or 43.3 per cent, were positive for rabies. Stray dogs, which were unavailable for examination, were responsible for exposure to rabies in 45 per cent of the patients treated. New Orleans experienced an epidemic of rabies beginning in the latter part of 1936 and continuing until the latter part of 1939. The present epidemic began early in 1943 and has shown a higher human mortality than the previous epidemic. Dogs were responsible for the exposure of 90 per cent of the patients treated and for all of the seven deaths from rabies. Actual injury by a proved rabid animal increases the mortality rate. Injuries about the face, head or neck are more dangerous than are injuries to other parts of the body. Injuries through clothing are less dangerous than injuries inflicted through the bare skin. The mortality from rabies is greater in Negroes than in white patients. Mortality from delay in instituting treatment is not significantly increased until two weeks after the injury. Rabies can be controlled by controlling the dog population.

North Carolina Medical Journal, Winston-Salem

5:413-476 (Sept.) 1944

Recent Experiences in Intensive Treatment of Syphilis. N. B. Hon.—p. 413.
Tropical Diseases in Returning Soldier. G. T. Harrell.—p. 416.
Endemic Typhus Fever: Report on 133 Cases. T. W. Baker and J. M. Alexander.—p. 421.
Radical Operation for Carcinoma of Ampulla of Vater and Head of Pancreas, with Report of Case. H. M. Schiebel and H. Sweaney.—p. 427.
*Carotenemia. V. S. Caviness.—p. 432.

Carotenemia.—According to Caviness, carotenemia is much more common than is indicated by the number of cases reported in the literature. He suggests that the condition is usually not recognized but is diagnosed as biliary jaundice. The chief differential points between jaundice and carotenemia are that: 1. There is no itching of the skin in carotenemia. 2. There is no yellowing of the scleras in carotenemia. 3. Yellowing of the skin in carotenemia is most intense in the palms and soles and about the nasolabial folds. In jaundice it is most intense in the scleras and on the trunk. 4. The urine in patients with jaundice is likely to show a deeper discoloration. 5. Urine chemical tests for bile should be positive in jaundice but negative in carotenemia. 6. In carotenemia there should be a high blood carotene level and no increase in the bilirubin content of blood; the blood bilirubin is high in jaundice. Icterus index changes, however, should be the same in the two conditions. 7. In carotenemia the stools are normal in color; in jaundice they are clay or putty colored. Cantarow and Trumper state that carotenemia occurs most commonly in children and diabetic patients, chiefly because of the prominent part that carotene containing vegetables occupy in their diet. Caviness reports the histories of 2 diabetic men who developed carotenemia. The first patient, a man aged 69, gave a history of having eaten large numbers of carrots daily. The second patient had lived for three weeks on a self prescribed diet of eggs. He was eating 27 eggs a day and was taking no other nourishment.

Northwest Medicine, Seattle

43:271-312 (Oct.) 1944

*Brucellosis, an Unrecognized Menace. R. R. Staub.—p. 274.
Orthopedic Aspects of Brucellosis. E. G. Chuinard.—p. 279.
Use of Stilbestrol in Carcinoma of Prostate. C. D. Donahue.—p. 284.
Psychogenic Asthma. S. Mayer Jr.—p. 287.

Brucellosis.—Staub states that less than 10 per cent of the patients with the chronic form of brucellosis have fever. Brucellosis is an important public health problem. Improved state and federal laws are necessary in the control, marketing and distribution of dairy products. A closer fraternity can profitably be developed between the medical and veterinary professions in the control of brucellosis and of other human infections contractible from animals. The medical profession must realize the unbelievable prevalence of brucellosis. The author thinks that 10 per cent of the population have brucellosis but that only about 1 per cent of infected persons are detected and treated. The sulfonamides are almost without value, although some believe that succinylsulfathiazole can benefit cases presenting early intestinal involvement. Penicillin shows only mild laboratory success. Fever therapy is more beneficial in acute than in chronic cases, especially in refractory cases not responding to vaccine therapy. Antiserum treatment is usually restricted to acute, severe attacks or exacerbations. Vaccine therapy seems

most promising in the treatment of acute and chronic brucellosis. The author uses a vaccine made only from the abortus strain. He prefers deep muscular injections and avoids subcutaneous injections. Vitamin therapy is an important supportive measure, as is also iron and liver. Thiamine hydrochloride seems especially beneficial in stimulating the production of opsonins, as does likewise the intravenous injection of nicotinic acid. Pentnucleotide and bone marrow are both used in cases of extreme leukopenia.

Public Health Reports, Washington, D. C.

59:1163-1194 (Sept. 8) 1944

Physical Impairments of Members of Low Income Farm Families—11,490 Persons in 2,477 Farm Security Administration Borrower Families, 1940: I. Characteristics of Examined Population. II. Defective Vision as Determined by Snellen Test and Other Chronic Eye Conditions. Mary Gover and J. B. Yaukey.—p. 1163.

59:1195-1238 (Sept. 15) 1944

Directory of Full Time Local Health Officers, 1943.—p. 1195.

59:1239-1266 (Sept. 22) 1944

Antiplague Measures in Tacoma, Washington. J. M. Hundley and K. W. Nasi.—p. 1239.

Rocky Mountain Medical Journal, Denver

41:609-696 (Sept.) 1944

Pitfalls of General Physician in Ocular Diagnosis. W. H. Crisp.—p. 626.
Salient Health Problems in Denver Area: Summary of Findings of Denver Metropolitan Planning Project. L. B. Byington.—p. 634.
Health Problems in Colorado. R. L. Cleere.—p. 639.
Introduction of Exotic Diseases into United States. L. Florio.—p. 643.
School of Medicine: Service to Doctors of Medicine in Colorado. M. H. Rees.—p. 648.

41:697-792 (Oct.) 1944

Medical Education and State Medical Society. E. R. Mugrage.—p. 714.
Reconditioning the Soldier Patient. A. Thorndike.—p. 718.
Newer Agents in Wound Healing (Antibiotics), with Particular Reference to Pencillin. F. B. Queen.—p. 721.

Southern Medical Journal, Birmingham, Ala.

37:533-596 (Oct.) 1944

Asymptomatic Heart Disease in Young Adults. J. E. Moss.—p. 533.
Complications Following Use of Antirabies Vaccine, with Suggestions as to Treatment. C. R. Thomas.—p. 539.
Infectious Mononucleosis in Negro: Report of 3 Cases, with 1 Complicated by Sickle Cell Anemia. E. S. Ray and R. C. Cecil.—p. 543.
*Infectious Mononucleosis of Unusual Severity, with Review of Jaundice Cases Occurring in This Disease. W. P. Boger.—p. 546.
Laboratory Tests in Study of Jaundice, with Particular Reference to Liver Function Tests. Eleanor W. Townsend.—p. 551.
*Vitamin K Therapy in Menorrhagia: Consideration of Hepatic Factor in Menstrual Disorders. R. Gubner and H. E. Ungerleider.—p. 556.
Incidence of Trichina Infestation in Eastern Virginia. A. C. Broders Jr. and W. B. Porter.—p. 558.
*Nutrition in Convalescence and Rehabilitation: Progress Report. T. D. Spies, R. W. Vilter and G. Douglas Jr.—p. 560.
Making Human Plasma Available for General Medical and Surgical Practice, with Particular Reference to Mobile Bleeding Unit as Means of Establishing and Maintaining Plasma Banks in Several Communities. J. W. Davenport Jr. and R. N. Chapman.—p. 573.
Metatarsal March Fractures. H. B. Kernodle and J. E. Jacobs.—p. 579.
Dual Plate, No Cast, Internal Fixation of Shaft Fractures. L. W. Breck and W. C. Basom.—p. 582.
Radiation Treatment of Ganglia of Wrist. R. J. Reeves.—p. 584.
Motor Driven Screw Holder—Screw Driver. G. R. Dawson Jr.—p. 587.

Infectious Mononucleosis and Jaundice.—According to Boger infectious mononucleosis is a protean disease whose only constant feature is an increase in the mononuclear elements of the blood at some time during its course. Those cases which present a sore throat and glandular enlargement are regarded as most typical and are diagnosed most frequently. A 19 year old boy presented many unusual features which are seldom encountered in the same patient, and the condition would undoubtedly have been erroneously diagnosed if a positive heterophile agglutination had not been obtained. Despite the gravity of the illness the treatment was purely symptomatic. The withholding of sulfonamide medication seems justified in the opinion of others, who have found that the sulfonamide drugs do no good in cases of infectious mononucleosis. The fever reached a height of 105.2 F. The authors thinks that the high temperature accounted for the patient's amnesia for a week of his hospitalization. The pertussis-like cough, which was so severe that it produced blood streaked sputum and hoarseness of the voice that has persisted for more than two months, is a feature of the disease which has not been commonly observed. Jaundice in infectious mononucleosis has been noted a number of times, but the mechanism of its production needs further investigation. Twenty-seven cases of jaundice are cited from the literature. The reported case illustrates the closeness with which infectious mononucleosis can simulate typhoid. The significant differential point was the generalized lymphadenopathy, which was not evaluated properly by reason of its having been found two and a half months prior to the onset of any acute symptoms.

Vitamin K in Menorrhagia.—Gubner and Ungerleider state that recent observations indicate that the liver is intimately concerned with the metabolism of the female sex hormones, and there is evidence to suggest that disturbances in liver function may be a factor in the genesis of some of the disorders of menstruation. Failure of the estrogen inactivating function of the liver may be contributory in the genesis of menorrhagia. Prothrombin formation occurs in the liver, and the level of plasma prothrombin is a sensitive index of the integrity of hepatic function. Vitamin K is intimately concerned with prothrombin formation, and its administration is indicated whenever prothrombin deficiency exists. Observation of striking improvement with vitamin K therapy in a case of severe menorrhagia with prothrombin deficiency led the authors to undertake an investigation of its therapeutic effect in a series of cases. Vitamin K was given to 43 patients with chronic dysmenorrhea and menorrhagia. No medication other than vitamin K was employed. The dosage varied slightly, averaging twenty 5 mg. tablets taken over a period of five days. Medication was begun in most cases one or two days before the onset of menstruation or on the first day of the menses. In 8 of 12 cases with a history of prolonged menstrual flow lasting six days or longer the duration of flow was reduced by one day or more. In the other 4 it was unchanged. In several women in whom spotting continued for ten or twelve days the flow was shortened to a normal length of four or five days. Of the 26 women in whom the flow continued for five days or less the duration remained unchanged in 16, was abbreviated in 8 and was prolonged in 2. Twenty-six of the women studied usually had clots during menstruation. The clots disappeared or diminished in 16 cases, were unchanged in 8 cases and increased in 2 cases.

Nutrition in Convalescence and Rehabilitation.—Spies and his associates state that persons with nutritive failure treated at Lakeside Hospital, Cleveland, had a deficient diet which was their only barrier to health and the ability to work. Unless something was done about the prevention of relapses in the treating of these chronically diseased persons, they continued to be dependent on their families or on social agencies. The authors report observations on 500 persons selected from a large group of patients who had recovered following treatment in the Nutrition Clinic. In most instances these patients gained strength promptly following nutritive therapy, but they were kept under close medical supervision until their health was restored and they were able to fulfil discharge requirements, the ability to do a full day's work every day. Precise diagnosis is the first step in shortening convalescence and hastening rehabilitation following nutritive failure. This is not easy, and no formula applies in every case. It is necessary to correlate the detailed information obtained from a nutrition history, laboratory determinations, physical examination and general medical history. The 500 persons rehabilitated or reconditioned included members of the armed forces and agricultural, domestic and industrial workers. The following four principles of nutritive therapy are recommended for shortening convalescence and rehabilitating persons who are ill solely from malnutrition: 1. The diet should provide 4,000 calories and should contain from 120 to 150 Gm. of protein and should be rich in vitamins and minerals. 2. Basic therapy should provide thiamine, riboflavine, niacin amide and ascorbic acid orally. 3. Synthetic vitamins should be given orally or parenterally. 4. Natural B complex should be given in the form of brewers' yeast or extract or rice bran extract and/or liver extract.

Surgery, St. Louis

16:319-476 (Sept.) 1944

*Myoblastoma. C. W. Howe and S. Warren.—p. 319.
Malignant Papillary Cystadenoma of Sweat Glands with Metastases to Regional Lymph Nodes. R. C. Horn Jr.—p. 348.
Experimental Observations on Human Ileocecal Valve. R. E. Buirge. —p. 356.
Papilloma of Gallbladder. W. Greenwald.—p. 370.
Urobilinogen Test as Additional Aid in Early Recognition of Fecal Fistula. I. D. Baronofsky.—p. 377.
Acute Physiologic Responses in Experimental Head Injury, with Special Reference to Mechanism of Death Soon After Trauma. E. S. Gurdjian and J. E. Webster.—p. 381.
Effect of Position on Shock Produced by Hemorrhage. A. Large. —p. 399.
*Spool Cotton as Suture Material. J. R. Floyd and M. J. Brockbank. —p. 403.
Cotton Surgical Suture Material. T. L. Hyde.—p. 407.
Survival of Rhesus Monkey Four Years After Excision of Head of Pancreas with Occlusion of External Pancreatic Secretion. A. Brunschwig.—p. 416.
Hemostatic Globulin and Plasma Clot Dressings in Local Treatment of Burns. L. Miscall and A. Joyner.—p. 419.
Translumbar Aortography: An Apparatus for Injecting Radiopaque Media. A. K. Doss.—p. 422.

Myoblastoma.—Howe and Warren report 10 cases of myoblastoma together with 44 cases collected by Klemperer and 104 additional cases collected from the literature. Myoblastoma is derived from embryonic myoblasts and may be distinguished from the rhabdomyoma group. Fifty-six per cent of the cases reviewed by the authors occurred in the upper respiratory and digestive tracts. Fifty-nine cases involved the tongue, and of these 3 were malignant. Eleven per cent of the total cases were malignant, and of these only 3 showed proved metastases. The authors think that whenever a myoblastoma is reported to have (1) atypism of cells, (2) excess mitotic figures, (3) spindle cell or sarcomatous pattern or (4) local invasion it should be treated surgically as a malignant tumor until more is known of the nature of these growths, especially if the patient is over 50 years of age. The degree of radiosensitivity and frequency of metastasis are as yet unknown. Both appear to be low. Tumors under the mucous membrane or the skin have a great tendency to be associated with hyperplasia and epidermoid carcinoma of the overlying epithelium.

Spool Cotton as Suture Material.—Spool cotton was the only suture material used by Floyd and Brockbank in 1,659 general surgical procedures. They believe that spool cotton is an excellent suture material for all types of general surgery, including clean and contaminated wounds. It is technically more difficult to handle than catgut and is thus conducive to painstaking surgery. It possesses minimal "foreign body danger." Induration, serum accumulation and postoperative wound infections are minimal with cotton.

16:477-632 (Oct.) 1944

*Prognosis in Acute Hematogenous Osteomyelitis With and Without Chemotherapy. W. E. Kenney.—p. 477.
Embolic Occlusion of Major Arteries. J. T. Reynolds and F. J. Jirka. —p. 485.
*Ligation of Aorta and Both Common Iliacs for Aneurysm: Report of Case and Review of Seven Operative Survivals of Aortic Ligation. D. T. Monahan.—p. 519.
*Physiochemical Disturbance in Severe Burn. B. J. Ficarra and E. A. Naclerio.—p. 529.
Leontiasis Ossea Complicated by Marjolin's Ulcer: Observation of Case for Twelve Years. R. E. Burger and E. P. Lehman.—p. 542.
Case of Spontaneous Gastrojejunal Fistula Eight Years After Operative Gastrojejunostomy. L. R. Kaufman and Helen I. Heiman.—p. 557.
Pantopaque: Notes on Absorption Following Myelography. G. M. Wyatt and R. G. Spurling.—p. 561.

Osteomyelitis With and Without Chemotherapy.—Kenney presents an analysis of the experiences of surgeons with 3,176 cases of acute hematogenous osteomyelitis. The mortality before the advent of chemotherapy was 23 per cent on the average, 46 per cent in the toxic cases and around 3 per cent in the nontoxic cases. After sulfonamide was used the mortality was 3.5 per cent. Previous to the use of sulfonamide, early bone decompression was almost prohibited by the severe mortality. Yet early bone decompression yielded the best results from the standpoints of the later integrity of the bone and function of the limb. Neither incision down to the bone, aspiration nor withholding operation either before or after the sulfonamides has given as satisfactory results as early bone decompression. The new drugs, by controlling the initial septicemia and that which may follow operative intervention, have now allowed safe, early procedures. The sulfonamide drugs have not proved of value so far as the local pathologic process is concerned. One must still depend on operation for the best results.

Ligation of Aorta and Both Common Iliac Arteries for Aneurysm.—Monahan says that Owings ligated the aorta of dogs in three stages, three weeks apart, and finally tied and severed the aorta; he was able in a small percentage of cases to have the animal survive in a normal state of health. His results encouraged Monahan to apply the same principle of gradual occlusion in a case of aneurysm of the aorta in the human being. Monahan occluded the aorta of a Negro aged 49 in stages by rubber bands proximal to an aneurysm with division of both common iliac arteries. The patient lived approximately five months from the time of the first ligation. Seven cases of aortic ligation are reviewed, 4 partial and 3 total. Of the 3 patients with total occlusions, 2 had collateral circulation established at the time of operation and the third had paralysis of the extremities following ligation and survived probably because of his youth. Occlusion of the lower abdominal aorta is feasible. Man will tolerate division of both common iliac arteries after ligation of the aorta. Cotton tape has been demonstrated as the least noxious material for ligation. It seems reasonable that ligation in stages with cotton tape, plus ligation of both iliac arteries, should cure aneurysms of the lower abdominal aorta.

Physiochemical Disturbance in a Severe Burn.—Ficarra and Naclerio made chemical analysis on a man aged 43 who sustained severe burns and who died on the tenth hospital day. The patient exhibited sodium chloride changes, hypoproteinemia, destruction of body protein, alterations in carbohydrate metabolism and hemoconcentration. The acidosis which usually accompanies the burn syndrome was absent. An unexpected alkalosis occurred following the administration of citrocarbonate on the fifth day after the burn. Emphasis is placed on a study of the blood chemistry on or about the fifth day. At this time a break in the biochemical harmony occurs. This discord is manifested in an elevation of the end products of nitrogen metabolism associated with a fall in serum proteins, plasma sodium and blood chlorides. Of 16,200 cc. of fluids administered parenterally, 6,900 cc. was of plasma and 3,100 cc. of whole blood. Death on the tenth day was attributed to adrenal exhaustion and renal failure. The major cause of death in burns has not been established satisfactorily. It is believed that a severely burned patient dies of physiologic exhaustion. Therefore a study of the organs involved in this disturbed physiology (liver, kidneys and adrenals) will assist in the elucidation of the unknown lethal factor. The exhaustion of the organs may be the cause of death when, after the second week, the patient seems to be improving. During the third week the initial danger apparently has been overcome. The anxious surgeon considers the patient sufficiently improved for a skin graft. However, the disturbed chemistry has not been restored. In the presence of this metabolic discord the administration of an anesthetic plus the surgical procedure may be sufficient to cause death. The thought is advanced that repeated examinations of the blood are necessary guides to the intelligent management and treatment of the severely burned patient. Whenever possible the laboratory studies should include a daily erythrocyte count, hemoglobin, urinalysis and blood chemistry determinations (proteins, sodium, chlorides, nonprotein nitrogen, icterus index and carbon dioxide combining power).

Wisconsin Medical Journal, Madison

43:1001-1100 (Oct.) 1944

Medical Care and Postwar Adjustment. C. Fidler.—p. 1025.
The Liver: A Symposium: 1. Some problems in the Physiology of Liver. F. C. Mann.—p. 1028.
Id.: 2. Studies of Liver Disease with Correlation of Clinical Features and Liver Function Tests. C. J. Watson.—p. 1033.
Id.: 3. Recent Trends in Surgery of Biliary Tract. C. W. Eberbach.—p. 1037.
Id.: 4. Jaundice and Its Surgical Aspects: Care of Jaundiced Patient Preoperatively and Postoperatively. M. A. McGarty. —p. 1043.
Id.: Discussion of Symposium. W. H. Cole.—p. 1048.
Post War: What Shall Medicine Do Then? Mary E. Switzer. —p. 1050.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Surgery, Bristol

32:1-108 (July) 1944

*Effect of Ligation on Infection of Patent Ductus Arteriosus. O. S. Tubbs.—p. 1.
War Surgery in Royal Air Force. S. Cade.—p. 12.
*Treatment of Burns and Wounds with Skin Loss by Envelope Method. R. P. Osborne.—p. 24.
Diagnosis of Depth of Skin Destruction in Burns and Its Bearing on Treatment. D. H. Patey and R. W. Scarff.—p. 32.
Recent Advances in Treatment of Carcinoma of Mouth and Jaws. T. H. Somervell.—p. 35.
Injuries of Urinary Bladder. J. C. Ross.—p. 44.
*Intraperitoneal Chemotherapy. R. H. Gardiner.—p. 49.
Shock: Consideration of Its Nature and Treatment. J. E. Dunphy.—p. 66.
Cholesteatoma of Petrous Bone. J. Pennybacker.—p. 75.
Adrenal Neuroblastoma. T. A. Ogilvie.—p. 78.
Local Sulfanilamide Treatment of Fresh Wounds in Complete Plasters. J. Orr-Ewing, J. C. Scott, F. H. Masina, J. Trueta and A. D. Gardner.—p. 83.
Miniature Scar-Carcinoma of Lung and "Upper Sulcus Tumor" of Pancoast. I. James and W. Pagel.—p. 85.
Adrenal Virilism: Report of Case with Unusual Features. N. G. B. McLetchie.—p. 90.

Effect of Ligation on Infection of Patent Ductus Arteriosus.—Tubbs states that the persistently patent ductus differs from that found at birth in being relatively shorter. It may have no length at all and be of the so-called window type. The frequency of complicating subacute bacterial infection is unknown. In the past the prognosis after the supervention of infection has been fatal with exceedingly few exceptions, the duration of life after the onset of infection varying from one month to two years. Nine cases of subacute bacterial endarteritis complicating a patent ductus and treated by ligation are described; 6 of these patients are well today, from fifteen months to over four years after the operation. The effect of ligation on infection of a patent ductus has been dramatic. Infection must now be considered an absolute and urgent indication for operation. It is important that the supervention of infection should be diagnosed early; any patient with a patent ductus who has an unexplained fever for more than two weeks should be suspected of this complication.

Treatment of Burns and Wounds by Envelop Method.—Osborne reports observations with this method in patients admitted to the plastic surgery and jaw injury service of the Stoke Mandeville Hospital. The 31 cases treated fall into three groups: 6 cases of new burns, 12 cases of old burns and 13 cases of unhealed wounds with loss of skin. The author used the tie-on type of Bunyan-Stannard envelop. Application is done under gas and oxygen or some other form of light anesthesia. The previous dressings are removed and a smear is taken for bacteriologic examination. Under a continuous stream of 1 per cent electrolytic sodium hypochlorite in tap water 1-5 at 110 F. the wound is cleansed with gauze swabs. All loose sloughs and destroyed soft tissue are removed. The area should be oozing blood at the end of ten to fifteen minutes after 5 to 8 pints has been used for a limb. Then a sterilized envelop sufficiently large to allow free movement of the limb is applied. The same solution is used for irrigating through the inlet, 5 pints being used for a limb. The solution is allowed to escape from the outlet as fast as it runs in so as to get the maximum chemical and mechanical effect. The envelop is allowed to drain for five to ten minutes. The interior of the envelop is dried by means of air blown through a sterile cotton wool filter by an electric hair drier or an electric suction machine. Adhesive seals are applied to the outlets and inlets. Subsequent irrigations are carried out without anesthesia, three or four times a day. Several case histories are given. Envelop therapy provides a reliable method of treating burns and wounds with full thickness skin loss. The method seems ideal for eliminating the hemolytic streptococcus and for reducing risk of cross infection to a minimum. Two other striking features have been the dramatic improvement of the general condition and the maintenance of full function.

Intraperitoneal Chemotherapy.—Gardiner believes that sufapyridine possesses advantages over other sulfonamides for intraperitoneal use. He has used sulfapyridine in all stages of acute appendicitis over the past two and a half years and the results have been gratifying. Seemingly hopeless cases of general peritonitis have resulted in rapid recovery, and many less advanced cases have done extremely well. Exudate was either reduced to a thin serous yellow discharge which did not last long or, if purulent, did not continue long. The author recommends the use of a fluid suspension, a solution not being possible owing to low solubility. The suspension is best made by rapidly stirring the finely powdered drug into sterile isotonic solution of sodium chloride. For 10 to 15 Gm. of powder about 6 to 8 ounces of the sterile fluid is necessary. The thin emulsion is best squirted rapidly into the peritoneal cavity with a 10 or 20 cc. record syringe. This method facilitates absorption and obviates adhesions. In the absence of pus or gross inflammation small doses suffice and 10 Gm. in 4 ounces of saline solution is adequate. The author generally uses 15 Gm. of sulfapyridine in 6 ounces of saline solution in contaminated cases. In cases with frank suppuration the author has inserted 25 Gm. of sulfapyridine with no toxic results. The complications, which are often troublesome when the drug is given by mouth or injection, have been entirely absent. Sulfapyridine shows the slowest absorption rate and the lowest toxicity of any of the sulfonamides so far employed for intraperitoneal use. Contaminated wounds treated with an emulsion of the sulfonamide powders will heal by first intention in the large majority of cases. Intraperitoneal chemotherapy should now be included in the armamentarium of all emergency surgeons.

British Medical Journal, London

2:297-328 (Sept. 2) 1944

Some General Considerations on Higher or Postgraduate Medical Studies. F. M. R. Walshe.—p. 297.
Use and Abuse of Trichlorethylene. G. E. H. Enderby.—p. 300.
Treatment by Movement. J. Cyriax.—p. 303.
Fatal Case of Mustard Gas Poisoning. F. B. Hobbs.—p. 306.
*Heparin in Intravenous Infusions, Including Penicillin Therapy. P. Martin.—p. 308.

Heparin in Intravenous Infusions Employing Penicillin.—Martin has recently used heparin in all infusions of blood (fresh or stored), plasma and solutions of crystalloids. The heparin is added to the infusing fluid by injecting it through the cork of the bottle by means of a hypodermic syringe. The amount used has been 1 unit per cubic centimeter of fluid—equivalent to 1 cc. of heparin per liter. Between 50 and 60 patients have received heparinized intravenous therapy. There has been no tendency to a recurrence of hemorrhage, and in postoperative cases there has been no evidence of bruising or hemorrhage in the area of the operation scar. In 8 cases the coagulation time was estimated before infusion and immediately afterward. In no case was there any significant alteration. It is suggested that heparin should be of value in preventing the thrombosis and phlebitis which are frequently seen when penicillin is given by intravenous drip. The impure solution of penicillin available at present irritates the endothelium of veins, causing phlebitis and a subsequent thrombosis. The author has in several cases employed heparin with penicillin. At first he used 1 unit of heparin per cubic centimeter of penicillin solution, but later 3 units per cubic centimeter was used. When the penicillin drip is 35 drops a minute, it does not seem possible to administer enough heparin to affect the clotting time.

2:329-362 (Sept. 9) 1944

*Retinal Detachment: Series of 78 Cases in Middle East Force. H. B. Stallard.—p. 329.
Nutritional Iron Deficiency Anemia in Wartime: Part III. Hemoglobin Levels of School Children and Pregnant Women in 1944, Compared with Levels in 1942 and 1943. L. S. P. Davidson, G. M. M. Donaldson, S. T. Lindsay and M. H. Roscoe.—p. 333.
Industrial Problems in Middle East. A. M. Critchley and I. H. Flack.—p. 334.
Classification of Deaths of Medicolegal Importance. I. Gordon.—p. 337.
*Specific Serum Therapy in Typhoid Fever. A. E. Hodgson.—p. 339.

Retinal Detachment.—Stallard presents observations on 78 officers and men of the Middle East force who had retinal detachment and were admitted to a military hospital in Egypt for treatment. Seventy-six were operated on; for 1 patient surgical treatment was not advised, and another made a spon-

taneous recovery. The operation was a combination of surface diathermy (90 to 100 milliampere for eight seconds) placed around the edges of a tear or tears and penetrating diathermy; one, two and very rarely more punctures were made in the sclera, with the diathermy needle carrying a current of 40 milliampere for one second. The interretinal fluid was sucked into a glass tube and rubber suction bulb applied to the sclera over the diathermy penetration. The 78 patients included 13 with cystic degeneration, 21 with choroidoretinal degeneration, 3 with myopia and 41 with trauma. The prospect of successful surgical treatment depends much on the type of case. The prognosis is reasonably good in early cases when the retinal tear is relatively small and easily accessible, the ocular tissues are in good condition, and an operation by a skilled surgeon is done within a month of the onset of the detachment. Large and multiple retinal tears are generally unfavorable, but not always so. The prognosis is slightly worse in deep detachments than in shallow ones on account of the distance of the retinal tear from the choroid. This is dealt with by passing penetrating diathermy needles through the sclera and choroid sufficiently long to reach the retina but not perforate it. Interretinal fluid drains away, and the detachment is shallower for subsequent diathermy applications. The prognosis is bad in long-standing cases. The incidence of success falls appreciably three months after the onset of detachment, but reattachment may occur after four and even ten years. Detachment on the nasal side is less serious as regards rapid extension than is detachment originating on the temporal side. The prognosis is bad in cases of retinal detachment associated with persistent inflammatory lesions of the choroid, sclera and orbital tissues (orbital cellulitis). Such cases are unfavorable for operation, and if an operation is done through mistaken diagnosis the condition is aggravated. Although the number of cases due to trauma peculiar to war is small (18 in this series) these few afford an indication of the seriousness of the prognosis and the difficulties which confront the surgeon in planning an operation on an eye which is often severely damaged as a result of either contusion or a penetrating wound or both.

Specific Serum Therapy in Typhoid.—Hodgson points out that the work of Felix and his colleagues at the Lister Institute made possible the elaboration of the Vi + O antityphoid serum, in which two antibodies are effectively combined, the Vi element conferring protection by suppressing the multiplication of virulent strains of Eberthella typhosa and the O antibody by neutralizing the endotoxin of that organism. This serum has been used in 57 cases of typhoid. Seven of the patients died, four deaths occurring within eighty hours of arrival at the hospital. Twenty of the patients disembarked at the port. These seaborne patients had mostly a severe type of typhoid. Patients who on admission showed toxic symptoms (general prostration, hyperpyrexia, threatened delirium, coma or typhoid state or complications such as hemorrhage or pneumonia), numbering 25 in all, received serum. Seaborne patients contributed 14 of the 25 serum cases and 4 of the 6 deaths. The patients not treated with serum were not controls but rather had mild infections. The serum is issued in 33 cc. phials, and injection of the contents of one phial intramuscularly (buttock) on three successive days was routine. In the very bad cases an initial dose of 66 cc. was given. This may seem a large amount for one intramuscular injection, but if the serum and the syringe have been previously warmed and kept in water at blood heat little discomfort is caused and absorption quickly takes place. Under the influence of the serum, conditions due to toxemia, excluding hyperpyrexia, abated rapidly, improvement appearing often within forty-eight hours and continuing to be sustained, with coincident decrease in signs and increase of strength and well being. Six of the severe cases were of the type for which, in other times, but little hope of recovery could have been entertained; they responded promptly. Hyperpyrexia was not affected so quickly, a fall in temperature taking some days and continuing as a moderately steep lysis. Complications such as intestinal hemorrhage or pneumonia, already present when the patient came under treatment, were not influenced by the serum.

Lancet, London

2:363-394 (Sept. 16) 1944

Plasma Fixation of Skin Grafts. J. E. Sheehan.—p. 363.
*Hepatitis After Yellow Fever Inoculation: Relation to Infective Hepatitis. G. M. Findlay, N. H. Martin and J. B. Mitchell.—p. 365.
Laboratory and Clinical Trials of Patulin. J. M. Stansfeld, A. E. Francis and C. H Stuart-Harris.—p. 370.
*Clinical Trial of Patulin in Common Cold. Report of Patulin Clinical Trials Committee Medical Research Council.—p. 373.
Simple Method of Amputating Thigh. C. W. G. Bryan.—p. 375.
Congenital Malaria in England. R. P. Gammie.—p. 375.

Hepatitis After Yellow Fever Inoculation and Infective Hepatitis.—Findlay and his associates could find no difference between the two conditions apart from the longer incubation period of postinoculation jaundice. This apparent discrepancy disappears when the incubation period of infective hepatitis following subcutaneous injection and the incubation period of postinoculation jaundice following intranasal instillation are considered. The authors describe epidemiologic and experimental investigations on infective hepatitis and on postinoculation hepatitis. They report possible examples of spread of postinoculation jaundice to contacts who had not been inoculated with icterogenic yellow fever vaccine. The incidence of infective hepatitis in childhood and adolescence in a sample of British troops has been ascertained. Evidence has been deduced that a previous attack of infective hepatitis gives a certain measure of protection against an attack of postinoculation jaundice, though the protection is not absolute. A complement fixation test has been developed the results of which tend to show that there is an antigenic relationship between the agents responsible for infective hepatitis and postinoculation jaundice. The authors also describe efforts to transmit postinoculation jaundice to man and to various animals. Evidence is accumulating that the agents responsible for infective hepatitis and the hepatitis that follows inoculation of icterogenic yellow fever vaccine behave in a similar manner and are antigenically related. Until knowledge has further advanced it would be idle to speculate whether these two agents are identical or merely members of a group of icterogenic agents one member of which is responsible for the production of infective hepatitis, a second for the hepatitis that is sometimes found in man after the injection of homologous blood or its products and a third, perhaps, for the jaundice in horses that follows the injection of homologous serum.

Patulin in the Common Cold.—The Medical Research Council reported in November 1943 on the chemical properties and clinical effects of a metabolic product of Penicillium patulum Bainier called patulin. It was shown in a clinical trial on the common cold in naval personnel that when 95 patients treated with patulin were compared with 85 controls the advantage to the treated patients was such that it would usually be regarded as statistically significant. Shortly after the publication of the first report an independent group of workers stated that they had been unable to demonstrate any effect of patulin on the common cold. The Medical Research Council undertook then an extensive reinvestigation of the claims regarding patulin. In a large clinical trial of patulin in widely distributed areas in Great Britain lasting from the beginning of December 1943 to the middle of April 1944 no evidence was found that patulin is effective in the treatment of the common cold.

Monatsschrift f. Geburtshilfe u. Gynäkologie, Basel

116:225-332 (Nov.-Dec.) 1943

*Significance of Diencephalohypophysial System for Production of Gonadotropic Hormones. A. Westman, D. Jacobsohn and N. A. Hillarp.—p. 225.
Frequency and Clinical and Etiologic Diagnosis of Ectopic Pregnancy. W. Dettling.—p. 251.
Effect of Estrogens on Anterior Pituitary Lobe of Avitaminotic Rats. C. A. Joel.—p. 277.
Effect of dl-Alpha-Tocopherol Acetate on Pituitary of E Avitaminotic Female Rats. C. A. Joel.—p. 288.
Experimental Studies and Clinical Experiences with Toxic Action of Natural Follicular Hormone and Synthetic Estrogen (Stilbene). K. Páli.—p. 297.

Diencephalohypophysial System and Production of Gonadotropic Hormones.—In order to investigate the relationship between the diencephalohypophysial system and sex function, Westman and his associates performed the following experiments on rats: (1) They completely separated the hypophysis from its infundibulum and the surrounding pars tuberalis, (2) extirpated the processus infundibuli and separated

the processus infundibuli from the infundibulum. In the animals of group 1 the pars distalis showed noticeable microscopic changes. The cells were uniform, and alpha cells were absent. The genital organs exhibited considerable atrophy. In the other two groups of animals in which the connection between the pars tuberalis and the pars distalis was left intact the pars distalis and the genital organs were normal. Determination of the volumes of the pars distalis in the different groups of animals indicated that the genital atrophy was not the result of the reduction in parenchyma. The authors emphasize that the connection between the hypothalamus and the hypophysis consists of two different parts. The one consists of the pars tuberalis with the portal vessels and a specific nerve fiber system; the other is formed by nerve tracts that pass from certain hypothalamic nuclei to the processus infundibuli and to the pars intermedia. The intact connection between the pars tuberalis and the pars distalis is the prerequisite for a normal production of gonadotropic hormones. The impulses which pass from the hypothalamus through the infundibulum and the processus infundibuli are of no significance for the sexual function. The authors think that the contradictory opinions about the significance of the diencephalohypophysial system for the sexual function are partly due to the fact that heretofore the functional differences between the two components of hypophysial attachment have been disregarded.

Medicina, Buenos Aires

4:391-516 (July) 1944. **Partial Index**

*Tests for Function of Adrenal Cortex. Drs. C. Galli Mainini; E. B. del Castillo, J. Reforzo Membrives and M. A. Gambin.—p. 391.

Tests for Function of Adrenal Cortex.—According to Galli Mainini and his collaborators the diagnosis of diseases caused by hyperfunction of the adrenal cortex is more difficult than the diagnosis of adrenal cortex insufficiency. They describe tests which they carried out on 16 patients with mild forms of adrenogenital syndrome and on the same number of normal persons. Adrenal hyperfunction manifests itself by metabolic disorders of the type which are seen in the Cushing syndrome, namely diminished elimination of chlorides, diminished dextrose tolerance, increased resistance to insulin, increased secretion of nitrogen after ingestion of carbohydrates and fats, and increased elimination of 17 ketosteroids in the urine. The clinical signs of adrenal cortex hyperfunction are sexual and metabolic, either alone or combined. The type of adrenal cortex hyperfunction with clinical symptoms of combined sexual and metabolic disorders is more frequent than that with symptoms of either sexual or metabolic disorders alone.

Chirurg, Berlin

15:345-375 (June 15) 1943. **Partial Index**

Treatment of Collapse After Spinal Anesthesia. T. von Matolesy.—p. 345.
*Procaine Hydrochloride Infiltration of Sympathetic Nerve in Early Treatment of Frostbites of Extremities. F. Bück.—p. 347.
Unusual Type of Calculus Disorder of Kidney as a Sequel of Fractures. H. von Brücke and O. Dobritz.—p. 352.
Sound Methods of Treatment of Gunshot Fractures of Femur. O. Wustmann.—p. 357.
Treatment of Gunshot Fractures of Femur and of Humerus. K. Ostermeyer.—p. 361.
Stable Extension and Gunshot Fracture. W. Rückert.—p. 362.

Procaine Infiltration of Sympathetic Nerve in Frostbites.—Bück states that paravertebral sympathectomy, stellectomy and periarterial sympathectomy are contraindicated in early treatment of frostbites because temporary functional impairment should not be combated by producing irreversible anatomic changes. Infiltration of the stellate ganglion with 1 per cent procaine hydrochloride solution in those cases in which the arm is involved, and paravertebral infiltration of the sympathetic nerve with the same solution in those cases in which the leg is involved, may be performed by any physician in any location and without any special equipment. Infiltration therapy was instituted in cases of fresh frostbite immediately after the cases had reached the author. Infiltration was first performed daily in grave cases and then every second day or at intervals of several days after improvement had been obtained. Bilateral infiltration was performed in cases of bilateral frostbite, and no untoward reactions occurred. Later on infiltration was performed alternately on one side, since a somewhat less accentuated effect was produced likewise at the counter side. From two to fifteen infiltrations were performed until clinical improvement was obtained, pain disappeared and oscillation tracings were restored to normal. Pains will cease immediately for from one to three hours after the first infiltration; they will be less severe and will disappear permanently after repeated infiltrations. Warming and reddening of the skin occur after the infiltration. Single, small, lightly red spots occur on the bluish extremities within five to ten minutes after the infiltration. Their number increases until the entire extremity becomes red except for areas in which the blood supply is definitely injured. Disturbances of sensibility and motor disturbances improved rapidly, sometimes after a single infiltration. A line of demarcation between the dead and the viable tissues became manifest after repeated infiltrations. Amputation should not be performed in the early stage. Moist gangrene did not occur in any of the author's cases. Extensive vascular changes may be prevented in addition to effecting a cure of the local acute frostbite.

Virchows Archiv. f. path. Anat. u. Physiol., Berlin

310:257-492 (May 4) 1943

Myocarditic Lesions in Horned Cattle With Hoof and Mouth Disease. K. Holz.—p. 257.
*Regeneration of Islands of Langerhans. L. von Bakay, Jr.—p. 291.
Deformity of Human Heart, with Special Reference to Bulbus and Truncus Arteriosus (Truncus Arteriosus Communis Persistens; Transpositions and Stenoses). W. Doerr.—p. 304.
Occurrence of Hemopoietic Tissue in Adrenal Gland of Man. H. Gormsen.—p. 369.
Pathologicoanatomic Study of Case of Cushing's Disease, with Recovery After Roentgen Therapy. K. Gaertner.—p. 388.
Occurrence of Malignant Tumors in Mice Following Autologous Transplantation of Normal Tissue of Mammary Gland. A. Fischer, with the assistance of G. Fischer, A. Bojsen-Moller and E. Middelboe.—p. 395.
Acute Yellow Atrophy of Liver in Children: Pathologicoanatomic Study of Epidemic Hepatitis. F. Roulet.—p. 436.
Physiologic and Pathologic Deposits of Fat in Liver of Domestic Mammals. Elfriede Overbeck.—p. 458.

Regeneration of Islands of Langerhans.—Microscopic studies by von Bakay revealed that the regenerative capacity of the islands of Langerhans is striking during fetal life. The capacity of a newborn infant who died during the delivery of a diabetic mother was manifested by the size of the islands, which had a diameter of 500 to 800 microns. The islands were surrounded by a strong capsule of connective tissue. This tissue formation was peri-insular in all the islands. A few argyrophile fibers were seen along the vessels inside the islands in only a few cases. A true glomus resulted from the dilatation of the capillaries inside the islands and represented another characteristic feature of the condition. The polymorphism of the nuclei was striking and was demonstrated by a large number of giant nuclei. Microscopic examination of 30 specimens from adults showed that postnatal island regeneration occurs under pathologic conditions in cases with impairment of the entire pancreas, i. e. in cases of true diabetes, chronic pancreatitis and pancreatic cirrhosis or in cases in which the functional disturbance results from circulatory insufficiency (arteriosclerosis of the pancreas). The absence of any clinical symptoms of diabetes may be explained by the compensating effect of an intensive regenerative process in the islands of Langerhans. In addition to the hypertrophy of epithelium in the excretory ducts, the increase in the insular system is due to the transformation of the acini and to the segmentation of the old islands. Traces of this regeneration could be found in almost all cases of diabetes. From 3 to 4 new islands were sometimes present adjacent to the proliferating excretory ducts. In 1 case the excretory ducts were considerably dilated as a result of the obstruction from the secretion; the high epithelium was completely flattened. The centers of the islands were pierced by dilated ducts. The origin of these islands from the ducts may be safely assumed. The regenerative tendency is suggested by the fact that in addition to the large hydropic islands others may be found which consist of small, dense, dark colored cells. They were surrounded by a ring of connective tissue which was thicker than that found in normal cases. Vessels are not found within these islands. Their rudimentary character explains the absence of clinical improvement in spite of the regenerative process which was demonstrated on microscopic examination. Regeneration in the head of the pancreas in a patient aged 65 suggested that the regenerative capacity is not reduced with advanced age.

Book Notices

Plaster of Paris Technic. By Edwin O. Geckeler, M.D., Associate Professor of Orthopaedic Surgery and Chief of the Fracture Service, Hahnemann Medical College and Hospital, Philadelphia. Cloth. Price, $3. Pp. 220, with 208 illustrations. Baltimore: Williams & Wilkins Company, 1944.

For a long time plaster of paris has been indispensable to orthopedic surgery. Calot considered plaster technic so important that he wrote "Show me your plaster . . . and I will tell you what kind of orthopedist you are." Descriptions of plaster of paris for immobilization are found in ancient history. Various forms of rigid bandages for immobilization were used as early as 1600 B. C. by the Egyptians, who applied gums and waxes to stiffen their surgical dressings in a manner similar to their method of embalming. More than a thousand years later Hippocrates described a similar method of treating broken limbs. The first use of plaster of paris for fractures was reported by Eton, who described a method in which solid gypsum was used by the natives of Basra; this material was poured over limbs in liquid form. In 1852 Matthysen, a medical officer in the Dutch army, described the use of gypsum bandages for treating the wounded in battle.

Although plaster bandages are used almost exclusively in the United States, pattern plaster is preferred by some surgeons abroad. In the latter form the plaster is laid over various parts of the body in shapes already cut out. The "closed plaster" method, popularized by Orr and Trueta, has saved countless lives and limbs in the present world war and permits early evacuation of the wounded with a minimum of hospitalization. The latest development in the use of plaster has been for severe burns. By the early application of plaster of paris to burned limbs, contractures and deformities can be prevented in many cases and minimized in more severe cases. On the modern battlefield plaster of paris can be applied in mobile units without the necessity of hospitalization. Good plaster bandages can be made by almost any one or several brands of ready made bandages may be purchased.

The combination of text and illustrations is a welcome contribution to the use of plaster of paris. It is an art to use plaster of paris skilfully. This book explains the art. The illustrations are unusually instructive. It is especially gratifying to find that such a monograph is suitable for the instruction of both graduate and undergraduate medical students. This book fills a definite need and undoubtedly will be used extensively. A practical knowledge of this work is not only valuable in everyday practice but is especially important in treatment of war injuries.

The Diabetic A B C: A Practical Book for Patients and Nurses. By R. D. Lawrence, M.A., M.D., F.R.C.P., Physician in Charge Diabetic Department, King's College Hospital, London. Eighth edition. Boards. Price, 4s. Pp. 69. London: H. K. Lewis & Co., Ltd., 1944.

The Diabetic A B C War-Time Supplement. By R. D. Lawrence, M.A., M.D., F.R.C.P., Physician in Charge Diabetic Department, King's College Hospital. Third edition. Paper. Price, 9d. Pp. 15. London: H. K. Lewis & Co., Ltd., 1944.

This edition of Lawrence's "The Diabetic A B C" is contained in two separate booklets: the manual, "A Practical Book for Patients and Nurses," and a wartime supplement. In the supplement the author demonstrates the means by which the diabetic patient can best meet the difficulties that war has imposed on him. Advice is given to the insulin patient who runs risks from air raids and invasion. The author takes cognizance of the special dangers during wartime to the patient whose life depends on insulin and by the withdrawal of which he would be subject to acidosis and coma. He also discusses in detail insulin supplies, food changes, emergency sugar ration, vitamins and the "Precautions for Diabetics in War-Time" as issued by the Ministry of Health in consultation with the Diabetic Association.

The wartime supplement is timely and of vital interest to all diabetic patients, and the author is to be highly complimented for presenting such vital aid in simple form to the patient and nurse.

In the introduction to "The Diabetic A B C" the author states that his book "The Diabetic Life" was written in scientific detail and contained much information unnecessary for the patient. The present reviewer, who also reviewed "The Diabetic Life," is in agreement with the author's opinion. Thus, in the "Diabetic A B C" the author now confines his reader to practical information which will aid him in cooperating with his doctor, to live more easily with minimum discomfort and to maintain better control of his diabetes. The details are adequately and simply discussed under diet-line-ration, a method of diet estimation which is popular in England but not in America. Also included are instructions about diet, recipes, insulin doses and their local reactions, insulin overdose and its effects, home life and traveling, as well as other important facts a diabetic patient should know. As was to be expected, this latest work of R. D. Lawrence is a masterful accomplishment of concision and unquestionable authority.

Structure and Function as Seen in the Foot. By Frederic Wood Jones, D.Sc., F.R.S., F.R.C.S., Professor of Anatomy, University of Manchester, England. Cloth. Price, $7.50. Pp. 329, with 150 illustrations. Baltimore: William Wood & Company, 1944.

This comprehensive monograph is purely anatomic, including comparative anatomy and biomechanics, i. e. function. The illustrations are profuse and highly instructive. The book will be of keen interest to anatomists and physiologists, and although there is no consideration of diagnosis or treatment it will be of much value to orthopedic surgeons. While many persons take a real delight in their hands, for the most part human beings have but little pride in their feet and it is unfortunate that this is so. The establishment of homologies between the bones, ligaments, muscles and other constituent parts of the hand and foot is an attractive study. It is one of the most delightful bypaths of comparative anatomy and has had a wealth of patient work devoted to it. The subject is of interest to every medical student. As an academic study the establishment of homologies has much to recommend it, but for the man who would treat the disabilities of the human foot it is far more important that his knowledge of the part should be of that intimate kind by which each bone, ligament, joint and muscle is known as an individual entity and not by reference to corresponding structures in other parts.

Manual of Psychological Medicine for Practitioners and Students. By A. F. Tredgold, M.D., F.R.C.P., F.R.S.E., Consulting Physician to University College Hospital, London. Cloth. Price, $5. Pp. 298. Baltimore: William Wood & Company, 1943.

This timely manual by the author of "Mental Deficiency" presents a description and methods of treatment of the various forms of mental abnormality. With the present wartime need for civilian physicians as well as psychiatrists in the armed forces to attack the problems of psychosomatic medicine and neuropsychiatric disorders it brings together in compact form a great deal of material comprehensive in scope. There are twenty-seven chapters ranging from introduction on the normal mind through classification, etiology, symptomatology, neuroses, psychoses, epilepsy and mental deficiency, and final chapters on legal relationships and sociological considerations. The book is written in a scholarly, yet clear and readable fashion; from the biologic approach it gives basic and essential information of value to the general practitioner as well as the clinical psychologist and psychiatrist. It is also recommended as a condensed textbook for medical students, who will find that it presents a thorough, logical and accurate description of the facts of psychiatry known today, thereby providing an excellent grounding in this specialty.

The Electrocardiogram: Its Interpretation and Clinical Application. By Louis H. Sigler, M.D., F.A.C.P., Attending Cardiologist and Chief of Cardiac Clinics, Coney Island and Harbor Hospitals, New York. Cloth. Price, $7.50. Pp. 403, with 203 illustrations. New York: Grune & Stratton, 1944.

Fundamentals are discussed in the first four chapters. The remaining twenty-one chapters are clinical. Frequent reference to original material reflects the personal experience of the author. Recent developments are well presented. Bibliographies following each chapter would be more useful if titles were included. Apical lead IVF is used in most illustrations. Sins of commission in legends to figures 28, 29, 31, 32, 76 and 118, of omission in 32 and 102, of speculation in 40 and 143 and of loose terminology in 36, 44, 60, 72, 73, 74 and 116 may confuse. The index is good. The price is high. Student and practitioner will find this book valuable and readable.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

MEASURING PHYSICAL FITNESS

To the Editor:—**I am interested in determining in as quantitative manner as possible a patient's fatigability. This is an individual who alleges disability because of extreme and undue fatigue. I am unable to find any objective testing methods in the literature more recent than the Schneider test of the first world war. Can you describe any newer testing procedures of value?**

M.D., Ohio.

ANSWER.—Valid and reliable measurement of the ability of a person to resist fatigue is more complex than is usually appreciated. The problems involved have received detailed attention and wide consideration since the beginning of the war. A basic introduction to the limitations and possibilities of such testing may be obtained from Burns, David: The Assessment of Physical Fitness, *Nature*, London **144**:466 (Sept. 9) 1939; Simonson, Ernst, and Enzer, Norbert: Physiology of Muscular Exercise and Fatigue in Disease, *Medicine* **21**:345 (Dec.) 1942, and Taylor, H. L., and Brozek, J.: Symposium on Physiological Aspects of Convalescence and Rehabilitation-Evaluation of Fitness, *Federation Proc.* **3**:216, 1944.

The simplest tests of fitness are cardiovascular and respiratory. Many have been described in the physiologic literature of the last two decades. In addition to the Schneider test, the best and most commonly used include the tests described by Crampton, C. W.: *Am. J. M. Sc.* **160**:721 (Nov.) 1920; Flack, M.: *Lancet* **2**:593 (Sept. 17) 1921; Turner, A. H.: *Am. J. Physiol.* **87**:667 (Jan.) 1929, and Master, A. M.: *Am. Heart J.* **10**:495 (April) 1935. Numerous motor performance tests may be found in the physical education literature. Representative examples appear in Brace's Measuring Motor Ability, New York, A. S. Barnes & Co., 1930. Recent additions should include Cureton's motor fitness screen test (THE JOURNAL, Sept. 11, 1943, page 69) and the numerous studies of Brouha and his associates (*New England J. Med.* **228**:473 [April 15] 1943; *Am. J. Phys. Anthropol.* **1**:95 [March] 1943; *Rev. canad. de biol.* **2**:86 [Feb.] 407, 1943; *Yale J. Biol. & Med.* **15**:657, 671, 679, 689 [May]; 769, 781 [July] 1943). The third type of test evaluates the ability to resist fatigue in terms of the response to sensory stimuli. The most recent development in this field is the fusion frequency of flicker measurement described by Simonson and Enzer (*J. Indust. Hyg. & Toxicol.* **23**:83 [Feb.] 1941).

There is no simple answer to this query. More would have to be known about the case history before specific testing procedures could be recommended as probably capable of reliably differentiating the abnormal person from the normal.

REFRACTORY PRURITUS VULVAE

To the Editor:—**A married woman aged 52 has had three attacks of pruritus vulvae within the past year. She was hospitalized during each attack for about three weeks. In addition to the intense itching there was severe pain which required an opiate to relieve. There was also a considerable degree of dermatitis extending upward and outward to the thighs. Therapy involved local applications of various ointments, hot packs, hot baths, douches, heavy doses of vitamins and x-rays; apparently nothing has given much relief. Can you suggest treatment for this condition?**

M.D., Virginia.

ANSWER.—It is assumed that a general physical examination has been made in this case and especially that the urine has been examined for the presence of sugar. The most common conditions which cause intractable itching in a woman 52 years of age are Trichomonas vaginalis vaginitis, moniliasis infection, kraurosis vulvae or leukoplakia, senile vaginitis, eczema and, of course, some general disorder such as diabetes, leukemia or Hodgkin's disease.

Naturally the treatment depends on the cause, if one can be found. Hanging drop examinations of the fresh discharge from the vagina or stained slides will reveal the presence of Trichomonas or Monilia if either one is present. Treatment of these afflictions nearly always brings relief from the itching, but recurrences are common. In kraurosis vulvae or leukoplakia the appearance will depend on the stage of the disease. In the first stage the vulva is swollen, red, bruised and painful. Later the tissues atrophy but the skin itself is thickened, indurated and leathery. Still later the skin becomes smooth and glistening and resembles parchment. The treatment of choice is vulvectomy both because other treatment is temporary and because in about half the women cancer will develop after a number of years. Temporary treatment with estrogens is most helpful and is the same as for senile vaginitis. In the latter condition the vagina is shorter and narrower than normal, and the introitus is considerably constricted. The mucosa is thinned out and easily traumatized. The best treatment is the use of estrogens to restore the senile vaginal mucosa to that of a normal premenopausal condition; but, unfortunately, the change is not permanent. In four to six weeks after the cessation of treatment the vaginal mucosa rapidly returns to its previous atrophic condition. It is best to treat women having senile vaginitis with an injection of 10,000 rat units (50,000 international units) of estrogenic substance once or twice a week for six or eight weeks. In addition, the patient should insert into the vagina every night a suppository containing 400 rat units (2,000 international units) of estrogenic substance. When itching is intense and the hypodermic and vaginal treatment do not relieve the pruritus quickly enough, a salve containing estrogenic substance should be prescribed. Usually relief is obtained within two weeks after treatment is started. If symptoms reappear, more injections of estrogen should be given. A number of courses may have to be administered. Uterine bleeding may result from this treatment, so the patient should be warned of this possibility.

If a medical disorder is found, specific therapy must be directed against it, of course.

In some cases which do not yield to local or endocrine therapy, the subcutaneous injection of alcohol may be tried according to the method of Jacoby (*Am. J. Obst. & Gynec.* **29**:604 [April] 1935). If this does not help, one may resort to resection of the sensory nerves of the vulva (Learmonth, Montgomery and Counseller: *Arch. Surg.* **26**:50 [Jan.] 1933) or a vulvectomy may be done.

HEMOSTASIS AFTER TONSILLECTOMY

To the Editor:—**Among the staff members at the local hospital there seems to be some difference of opinion as to the proper method of hemostasis after tonsillectomy. Most of them pay little attention to bleeding from the tonsil fossa unless it is profuse. Venous oozing of a small amount is more or less ignored. The intent seems to be to finish as soon as possible, without much concern for a dry field. Other doctors contend that hemostasis should be as complete as for any other operation and that the field should be completely dry before finishing. The first group contends that venous oozing from a raw surface, as the tonsil fossa, is natural and that it will stop spontaneously after the operation, which is true in most cases. Isn't post-tonsillectomy hemorrhage, within eight hours, much less likely to occur if hemostasis has been complete? What percentage of these hemorrhages is the direct result of failure to secure a dry field at the time of operation? Is there tonsillectomy hemorrhage, within the first eight to twelve hours in (a) children and (b) adults? In this connection there is also a difference of opinion as to the proper use of a La Force tonsillectome with hemostatic and cutting blades. One group of doctors leaves the hemostatic blade clamped down, only long enough to remove and inspect the tonsil. The other group leaves the hemostatic blade clamped for three to five minutes, contending that hemostasis is better. Which technic is the better? What are the most satisfactory hemostatic agents for topical application to the tonsil fossa to control bleeding? An early reply will be appreciated.** **M.D., Utah.**

ANSWER.—There should be no great difference of opinion as to the necessity for stopping important bleeding in the tonsillar fossae after tonsillectomy. The only room for debate will be in those cases in which the bleeding is obviously slight. Here it is true that many will rely on experience, which indicates that most of the time this will stop spontaneously. There are others, however, who insist on a dry fossa being present before a patient is allowed to leave the operating room. This care is to be commended, and there is good reason to believe that those who follow this practice will have much less bleeding which requires attention. That this is so may not be apparent over a short period of observation, nor will it seem to be so in the practice of an occasional operator. Such care is rewarded in the diminished number of patients who will lose noteworthy amounts of blood, in the smaller number of persons requiring a second anesthetic to carry out this procedure and in undesirable psychologic reactions, particularly in children, who do not take kindly to the necessary handling.

It is not possible to give accurate statistics as to the frequency of primary tonsillar bleeding (i. e. that occurring any time in the first twenty-four hours after operation). It will vary with different methods with different operators and perhaps with different seasons and parts of the country. It has been reduced in the practice of some to much less than 1 per cent. So too the percentage of hemorrhages occurring as a result of failure to secure a dry field cannot be determined; for who attempts to gather such figures or who will admit negligence? The important thing is that the surgeon doing tonsillectomies is bound no less than the general body of surgeons to observe the rules that apply throughout this field to the control of bleeding. Hemostasis is an important part of the discipline of surgery, and laxity should never be permitted.

Primary hemorrhage (i. e. that occurring within the first twenty-four hours) occurs both in children and in adults.

The crushing blade of the La Force tonsillectome should be left on for a few minutes before the cutting blade is used, for that is the rationale of its use, namely that crushing tissues promotes hemostasis.

There are many agents for topical applications to the tonsil fossae after operation. A satisfactory one is made of tannic acid crystals to which enough epinephrine hydrochloride solution (1 : 1,000) is added to give a consistency of mustard. Some use gallic acid crystals and others a mixture of equal parts of the two. The iron salts also have been and are popular in various solutions. They leave an undesirable eschar, however, and the tannic acid preparations described are perhaps more desirable. This is especially true if one considers that topical applications cannot be depended on to stop bleeding of note. They are useful for stopping trivial oozing. All other types of bleeding should be handled in the accepted surgical fashion, namely by pressure, clamping or the judicious use of the ligature.

PYREXIA OF UNDETERMINED ORIGIN

To the Editor:—A boy aged 9 has had a low grade fever for the past three years (98.6 to 100.8 F. by mouth). The present illness began with a sudden severe tonsillitis and bronchitis; the fever, which was high, lasted for three weeks. He has continued to have the low grade fever since then. He had lobar pneumonia at the age of 1½ years and measles following "intestinal flu" at 2½. Raw milk has been used at different intervals since the age of 2. Physical examination is normal except for height, 54½ inches (138 cm.), and weight, 83½ pounds (38 Kg.). Examination of the heart reveals a soft systolic mitral murmur not transmitted, which has not increased during the past two years. Laboratory examination showed red blood cells 5,200,000, hemoglobin 15 Gm., white blood cells 8,600, polymorphonuclears 55, lymphocytes 41, monocytes 2, eosinophils 1 and transitional cells 1. The sedimentation test, repeated several times, gave a rate of 10 mm. in one hour. The urine is normal. The results of the tuberculin test from 1: 1,000 up to 1 mg. were all normal. Agglutination tests for typhoid, Brucella abortus and Brucella melitensis were normal; there were no heterophile antibodies. Examination of the blood chemistry revealed cholesterol 235, chloride 615, calcium 10.8, phosphorus 4.0, total protein 6.72, sugar 90 and Weltman 9. Negative cultures were obtained from the blood, urine, nose; throat showed pneumococcus, Micrococcus flavus and gamma streptococcus. A skin test performed with Brucella melitensis with 1: 1,000 dilution was negative with negative control; with 0.1 cc. of full strength, the test was positive, with negative control. A chest plate gave a normal result; the heart is normal in size and outline. X-ray examination of the accessory nasal sinuses revealed no abnormality. Is a diagnosis of brucellosis justified? If so what treatment is recommended? Has rheumatic fever been ruled out? Should tonsillectomy be performed because this child has two or three severe attacks of tonsillitis a year? Have you any further suggestions for work-up of this case?

William F. Mahaney, M.D., Saco, Maine.

ANSWER.—If the patient is well, active and gaining weight and height normally, there may be no need for particular concern. The boy's temperature, which is higher than the average, may be normal for him and not "fever" at all (Reimann, H. A.: The Problem of Long Continued Low Grade Fever, THE JOURNAL, Oct. 3, 1936, p. 1089). He is taller and heavier for his age than the average, but the cardiac murmur is probably not of significance. However, as in all cases of this type, continued unobtrusive observation is wise.

The history of repeated respiratory tract infections beginning in infancy brings up the possibility of bronchiectasis in spite of the normal roentgenogram. If cough with sputum develops, it may be desirable to make a bronchogram after injecting iodized oil. If he has chronic brucellosis one would not expect such an evenness of fever for three years but rather remissions, slight relapses and other signs and symptoms. Furthermore, brucellosis cannot be diagnosed solely from a positive skin test. Without other evidence, rheumatic fever is also an unlikely diagnosis.

A history of repeated attacks of severe tonsillitis is the prime and almost only indication for tonsillectomy generally; if actual tonsillitis continues to recur in this patient, the tonsils should be removed.

NEW "CURES" FOR LEUKEMIA

To the Editor:—Is there any new drug that is of benefit in the treatment of an acute lymphatic leukemia? While in Chicago I noticed in one of the daily papers that some new drug was being used on a patient in Ohio, but the press did not mention the name of the preparation.

Bernard J. Baute, M.D., Lebanon, Ky.

ANSWER.—There is no new drug which offers any hope in the treatment of acute leukemia. Reports of cures or new treatments for leukemia appear frequently in the press. The index of one large newspaper contains seven reports of new treatments for leukemia in the past six years; none of these have proved successful. If a specific agent for leukemia is discovered, it would undoubtedly receive prompt recognition in THE JOURNAL.

PAINFUL AXILLARY MASSES IN PREGNANCY

To the Editor:—A woman aged 23 is now fourteen weeks pregnant. When she was about eight weeks pregnant she began complaining of pain and swelling in the right axilla. A few weeks later the axilla became swollen and painful. The mass in the right axilla is about the size of a large lemon, while that in the left is about the size of a hen's egg. Both masses are tender to pressure, and because of the pain the patient is forced to sleep on her back. I can find no suggestion of a nipple or other opening in the region of these masses. I have had 2 patients in the past with swollen axillary masses, but they were not apparent until a few days prior to delivery and promptly subsided shortly after delivery, owing, I think, to not allowing the mothers to nurse the babies. What treatment would you suggest? Is it good practice to remove this tissue surgically?

M.D., West Virginia.

ANSWER.—The masses described are almost certainly accessory mammary tissue which are stimulated to grow by the hormones produced in pregnancy. Generally these masses give no trouble until after delivery, but not infrequently they are distressing during pregnancy. There is no need for surgery. In some cases the administration of diethylstilbestrol reduces the size of the swellings and the pain they cause. The patient may be given 5 mg. of any one of the Council accepted commercial preparations morning and night for five days. It may be necessary to repeat such a course of therapy one or more times during pregnancy and in the puerperium. The results are comparable to the relief of congestion and pain in the breasts during the first few days post partum obtained by the use of diethylstilbestrol.

MERCURIAL DIURETICS FOR PATIENT WITH CONGESTIVE HEART FAILURE

To the Editor:—A man aged 56 has hypertensive cardiovascular disease. His cardiac reserve has been diminishing in the past two years. He now develops massive edema of the legs, and some fluid collects in the abdomen and chest. This can be made to disappear with a few intramuscular injections of salyrgan and theophylline, but soon recurs. Is it safe to continue using the salyrgan and theophylline two or three times a week to keep his edema down? His urine has 3 plus albumin but no cells nor casts. His edema cannot be controlled by bed rest and digitalis. He is uncomfortable when the fluid collects and has to sit in a chair at night. When the fluid is gone he is fairly comfortable.

M.D., New Jersey.

ANSWER.—It is considered safe to inject a mercurial diuretic more than once a week and for an indefinite period as long as the patient responds with a satisfactory diuresis. It is assumed that the patient is on a salt poor diet and restricted as to fluid intake. The presence of albuminuria is not a contraindication to the use of mercurial diuretics for a patient with congestive heart failure; neither is the presence of a moderately elevated nonprotein or urea nitrogen in the blood, provided the creatinine is normal. If ammonium chloride is used in adequate dosage (6 Gm. daily in enteric coated capsules) the number of mercurial injections may be reduced to less than two a week.

PHYSICAL INFLUENCES ON LOCALIZATION OF SKIN LESIONS

To the Editor:—A boy aged 6 years was injured in a fall and received a simple fracture of the left radius without displacement. A supporting plaster splint was applied from just below the elbow to the palm and held in place with a muslin bandage. No stockinet or other material was used between the skin and the plaster. The splint was worn continuously for about three weeks, after which it was worn during the day for protection only. About four weeks after the injury the child developed chickenpox and the splint was removed. The rash was fairly heavy and evenly scattered except for that part of the left forearm which had been in contact with the plaster. Over this area the lesions were exceptionally numerous. The illness took the usual course and there were no complications. A dark suntan was present over the upper half of the body except the part of the left arm covered with the bandage. The lesions on the extensor surface of the forearm where only the muslin bandage had covered the skin were no more numerous than elsewhere. What is the basis for the predilection of the pox for the skin area which has been in contact with the plaster splint, even though the splint was not worn after the rash began to appear? Ira D. Hirschy, Major, M. C., A. U. S.

ANSWER.—Every dermatologist is familiar with instances of peculiar localization and distribution of lesions determined by physical means. Sometimes the influence of these agents is felt long afterward. This has given rise to the expression that the skin has a long memory. An area of sunburn, zones of pressure from suspenders, the site of a chemical irritation or points of trauma may be the ones where a future eruption does or does not occur. It has come to be accepted, though not fully understood, that the skin may be sensitized by substances such as poison ivy resin. The apparently normal skin between attacks harbors invisible changes that give it certain potentialities. In some manner also physical agents unquestionably leave a durable impress on tissues. What these changes are and how they occur is much less understood than even the phenomena of allergy.